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Utility of the estimation of Adenosine Deaminase (ADA) level in diagnosis of Tuberculosis

S K Baruah*

“ In the future, what is tuberculosis and what is not will not be difficult. The demonstration of tubercle bacilli will settle the question.”

Robert Koch, 1882

In the body fluids, demonstration of Tubercle bacilli is a challenging task for the clinicians. Another unresolved issue is that of Sputum negative pulmonary tuberculosis, particularly so when the chest X-Ray is not suggestive. In these situations, the estimation of Adenosine Deaminase (ADA) levels in different body fluids as well as Broncho Alveolar Lavage (BAL) fluid gains utmost importance. ADA levels are utilized for diagnosis of Tuberculosis in different locations. Although many studies have evaluated ADA levels in several locations, there is no consensus about a definite cut-off level as different laboratories practice different levels. However, it is clear that ADA levels are higher in Tuberculosis of different body fluids. ADA levels can supplement Clinician's suspicions about tuberculosis and arrive at a diagnosis.

Adenosine Deaminase (ADA) is an important enzyme that catalyzes the deamination of adenosine and deoxyadenosine into their respective inosine nucleosides.^{1,2} This conversion is an initial step of a series of reactions responsible for lymphocytes proliferation and differentiation. Therefore, ADA is considered as an indicator of cellular immunity and fundamental for the differentiation of lymphocytes.³ ADA is raised in several diseases, like lymphocytic effusions, including those consequent of tuberculosis, neoplasms and some acute

viral infections. This suggests that a high ADA activity is indirectly related to the subsets of T cell lymphocytes involved in the inflammatory response.⁴ Determinations of ADA levels in pleural fluid may be useful adjunctive tests in the diagnosis of pleural fluid; their utility in the diagnosis of other forms of extrapulmonary TB (e.g., pericardial, peritoneal, and meningeal) is less clear.⁵ However in one study, it was reported that in tubercular, pleural, pericardial and peritoneal effusion, an ADA cut-off value of 40 IU/L has a sensitivity and specificity of 100% and 94.6% respectively.⁶

In Ascitic fluid, a value of >31 U/L has sensitivity, specificity, positive and negative predictive value of 100%, 92%, 72% and 100% respectively.⁷ In another study, it was reported that a cut-off value of 41.5 IU/L has a sensitivity, specificity, positive and negative predictive value of 80%, 97.2%, 82.9% and 88.6% respectively in tubercular peritonitis.⁸ In a meta-analysis, a value of 36-40 IU/L of ADA levels in peritoneal tuberculosis showed a sensitivity of 100% and specificity of 97%.⁹ In CSF, a value of more than 3.30 IU/L has a sensitivity and specificity of 100% and 97.87% respectively.¹⁰ In another study, it was found that a CSF-ADA cut-off level of 6.5 IU/L has a sensitivity and specificity of 95.83% and 92.85% respectively.¹¹

Another important issue is that of sputum smear negative cases of pulmonary tuberculosis, where Chest X-ray is inconclusive. Here, the determination of ADA levels in Bronchoalveolar Lavage (BAL) fluid plays an important role. In one study, the mean ADA level in BAL fluid was 4.13 ± 2.55 IU/L in Tuberculosis group of patients.¹² Using a cut off value of 3.5 IU/L, the sensitivity and specificity were 57% and 84% respectively. The

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results showed that although ADA activity in BAL fluid of pulmonary TB patients was higher than those seen in other diseases, a negative test does not rule out pulmonary TB.¹³ In another study, BAL fluid ADA was found to be much higher ($P < 0.001$) in sputum negative pulmonary tuberculosis compared to the controls with a sensitivity and specificity of 100% and 85.3% respectively.¹⁴

Although, higher level of ADA in BAL fluid is very helpful in diagnosis contributing to Clinician's suspicion of sputum negative pulmonary tuberculosis particularly when the X-Ray is inconclusive, it requires a special set up where Bronchoscopy is available. It adds to the cost, a part of which has to be borne by the patient. It may not be possible in India, where a large number of tuberculosis patients are present, to access the specialized centers where Bronchoscopy is available. A ray of hope for these patients is the scaling up of Cartridge Based Nuclie Acid Amplification Test (Gene Xpert), a real time PCR test, undertaken by the Revised Nation Tuberculosis Control Programme, under Central TB Division, Government of India. However, in case of routine diagnostic Bronchoscopy, estimation of ADA levels in BAL fluid, along with other diagnostic tests, may be helpful to detect or exclude sputum negative pulmonary tuberculosis.

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Role of ADA in bronchoalveolar lavage fluid in the diagnosis of sputum smear negative pulmonary tuberculosis

B Hazarika*, K R Sarmah**, S Medhi***, J Sarma****

Abstract

Background: Sputum smear negative pulmonary tuberculosis still remains a diagnostic challenge to physicians despite the development of newer and rapid laboratory tests for the diagnosis of this ancient killer, which has continued to cripple humanity since time immemorial. Sputum smear negative pulmonary tuberculosis remains a diagnostic dilemma and rapid and cost effective methods are required for early diagnosis and treatment, and thus prevention of transmission of this highly communicable disease. This study aims to evaluate the role of ADA in BALF in detecting sputum smear negative Pulmonary tuberculosis. **Materials and methods:** An institutional based prospective study was undertaken in the department of Pulmonary Medicine, Gauhati Medical College and Hospital, Guwahati, Assam from June 2014 to December 2014 with 63 clinically and radiologically suspected cases who were sputum smear negative. Flexible fiberoptic bronchoscope was done in these patients; excluding contraindications of broncoscopy and BAL fluid was obtained from a pulmonary lobe with the most involvement seen on chest X-ray/CT thorax and a right middle lobe in patients with a diffuse involvement. The diagnosis of pulmonary tuberculosis was confirmed by AFB culture of the BALF or post bronchoscopy sputum. ADA was assayed by Giusti's colorimetric method and values measured and compared with the different groups. **Results:** Out of a total of 63 patients, 25 patients (18 males, 7 females; mean age: 64.06 ± 19.37 years) had pulmonary TB, 23 (13 males, 10 females; mean age: 56.18 ± 18.60 years) had non-TB lung disease and 15 cases (10 males, 5 females; mean age: 42.13 ± 21.45 years) were taken as controls. The mean ADA value was found to be 6.95 in the confirmed cases of pulmonary tuberculosis; which was statistically significant. Compared with the other groups, the test had a Sensitivity of 76%; specificity of 61%; PPV was 65.52% and NPV was 68.42%. **Conclusion:** Thus this study showed that ADA level was significantly higher in TB patients than in the other two groups ($p < 0.05$) and can be a useful diagnostic tool in high prevalence countries like India. Further large scale studies are recommended to confirm our findings.

Key words : Adenosine deaminase, Bronchoalveolar lavage,

INTRODUCTION :

Tuberculosis (TB) remains one of the world's deadliest communicable diseases. It is a major global health problem, responsible for ill health among millions of people each year. TB ranks as the second leading cause of death from an infectious disease worldwide, after human immunodeficiency virus (HIV)¹. Although the developed countries have seen a considerable decline in the incidence and prevalence of pulmonary tuberculosis, it is still a major cause of morbidity and mortality in developing countries like India. India is the highest TB burden country in the world with WHO statistics for 2013 giving an estimated

incidence of 2.1 million cases out of a global incidence of 9 million and a prevalence of 2.6 million cases².

We still rely best on the results of sputum smear microscopy, the age old diagnostic test for detecting pulmonary tuberculosis and as mentioned earlier the advent of newer diagnostic methods has not been able to surpass the impact of sputum smear microscopy and AFB culture which is considered the gold standard. But the major drawback of this test is that, sputum smear microscopy maybe negative in 22 to 61% of cases³.

AFB culture on Z-N media is time consuming and takes about 4 to 6 weeks time. This population of sputum smear negative cases or those who do not produce sputum, but are highly suspicious clinically and radiologically remain in the gray zone presenting a dilemma to the physician whether to start antitubercular drugs empirically or wait and allow the disease to progress.

Several biomarkers like adenosine deaminase (ADA), interferon gamma (IFN- γ) and a variety of tumor

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markers and cytokines have been proposed as alternative non-invasive means of establishing tuberculous aetiology. There is sufficient data supporting the yield of ADA in various body fluids for the diagnosis of extrapulmonary tuberculosis like pleural, pericardial, ascitic fluid, CSF etc. However, few studies have been done to assess ADA activity in bronchoalveolar lavage (BAL) fluid and its diagnostic value is still unknown.

Adenosine deaminase (ADA) has been developed and widely used for the diagnosis of TB due to its simplicity, low cost, and quickly available results. Many studies have confirmed the high sensitivity and specificity of ADA (sensitivity 92% and specificity 89%) for early diagnosis of extrapulmonary tuberculosis such as tuberculous pleuritis, pericarditis, ascites and meningitis⁴. ADA is an enzyme catalyzing the deamination reaction from adenosine to inosine. It is also an essential enzyme of the purine catabolic pathway. ADA acts in proliferation and differentiation of lymphocyte, especially T lymphocyte. It also acts in maturation of monocytes transforming them to macrophage. ADA is a significant indicator of active cellular immunity. It increases in biological fluids in the course of infectious disease characterized by micro-organisms infecting the macrophages. The levels of ADA increase in TB because of the stimulation of T cells by mycobacterial antigens⁵.

The aim of this study was to evaluate ADA activity in bronchoalveolar lavage fluid in detecting pulmonary tuberculosis in clinically or radiologically suspicious cases who are sputum smear negative or are unable to expectorate sputum.

MATERIALS AND METHODS :

An institutional based prospective study was undertaken in the department of Pulmonary Medicine, Gauhati Medical College and Hospital from June 2014 to December 2014. Demographic data (including age, sex, occupation and smoking status) and clinical data (including presenting symptoms, underlying diseases, HIV status-if available, clinical diagnoses and radiographic patterns) were collected. Sixty three patients, with suspicious clinical and radiological features for pulmonary TB, who were either sputum smear negative (atleast 2 samples) or unable to expectorate sputum were enrolled in the study. Patients >12 years of age, willing to give

consent, who had cough for more than 2 weeks, hemoptysis, evening rise of temperature or patients with clinical and radiological features suggestive of pulmonary tuberculosis but sputum smear negative were included in the study. Patients with contraindications of bronchoscopy like Hypoxia ($spo_2 < 92\%$ at room air), patients with associated malignant arrhythmia, unstable cardiac status, patients with bleeding diathesis and unconscious patients were excluded.

Fibreoptic bronchoscopy was used to obtain BAL samples. The patient was called nil per orally in the morning and nebulised with 4% lignocaine solution for about 15 to 20 minutes. It was performed with the patient in supine position, through transnasal route or transoral route in special circumstances; with pre procedure assessment for BP, ECG and pulse oximetry. Oxygen saturation was monitored all throughout the procedure with an aim to maintain saturation at >92%. Stepwise examination starting from glottis, trachea, carina was done, then the normal side bronchial tree was examined first and adequate BAL sample taken from the radiologically suspected abnormal lobe. To obtain BAL fluid, 100 cc normal saline was injected through five 20ml aliquots wedged into a subsegmental bronchus and the returned fluid was collected via suction and sent to the laboratory for AFB culture and ADA test. Post bronchoscopy sputum was also sent for AFB culture. After the procedure patients were observed for potential complications and advised to be on empty stomach for another two more hours.

DIAGNOSIS :

Those patients who had positive results for post bronchoscopy sputum cultures or BAL cultures for AFB were considered as definite case of pulmonary tuberculosis. Culture for AFB was done in Lowenstein-Jensen medium. Those who had other forms of pulmonary diseases and were negative for TB were included in the non-TB lung disease group. Individuals, in which TB and other pulmonary diseases were ruled out, were selected as the control group.

ADA ASSAY :

To assess ADA activity, the samples were centrifuged and kept at 21 degree C. Then ADA levels in BAL fluids were compared to each other by ADA kit. ADA activity

was measured by Giusti's colorimetric method. By this method, ADA activity can be measured up to 100 IU/L.

STATISTICAL ANALYSIS :

Data were analyzed by independent t-test; ROC curve and area under ROC with 95% confidence interval was calculated using SPSS software 11.5. p value of < 0.05 was taken as significant.

RESULTS :

Among the 63 patients enrolled in this study; 25 patients (18 males, 7 females; mean age: 64.06 ± 19.37 years) had pulmonary TB; 23 (13 males, 10 females; mean age: 56.18 ± 18.60 years) had non-tubercular lung disease and 15 cases (10 males, 5 females; mean age: 42.13 ± 21.45 years) were taken as controls. BAL for AFB culture or post bronchoscopy sputum culture was positive in the 25 patients in pulmonary tubercular group. In the two other groups, BAL culture or post bronchoscopy sputum culture were negative for AFB. In the non-tubercular group, there were a total of 23 cases, out of which 9 cases were bronchogenic carcinoma, 7 cases were post tubercular sequelae/bronchiectasis, 4 cases of sarcoidosis, 3 cases of necrotising pneumonia. 15 apparently normal subjects were taken as control.

Table 1: Demographic data

	Pulmonary tuberculosis	Non-tubercular other lung disease	control
Total patients	25	23	15
Mean age	64.06+/- 19.37	56.18+/- 18.60	42.13+/- 21.45
Males	18	13	10
Females	7	10	5

The mean ADA level was found to be higher in the pulmonary tuberculosis group than in the non-tubercular other lung diseases and control groups.

Table 2: Mean ADA levels and standard deviation among the three groups

	Mean	SD	n
PTB	6.95	6.82	25
Non-PTB	3.34	4.42	23
Control	2.92	1.86	15

There was a significant difference in the p values when compared between pulmonary tuberculosis and non-tubercular other lung disease group, and also between pulmonary tuberculosis and control subjects. But no significant difference was found in BALF ADA levels between the non-tubercular other lung disease group and control.

Table 3: p values

	p value	
PTB and non-tubercular	0.0364(p< 0.05)	significant
PTB and control	0.0318(p< 0.05)	significant
Non-tubercular and control	0.73(p> 0.05)	Not significant

To determine the best predictive value of ADA level, ROC curve (with 95% CI) was used which did not show a significant difference. At the designated cut-off level of 1.65 IU/L, the highest sensitivity and specificity for diagnosis of tuberculosis were found. Sensitivity 76%; specificity 61%; PPV 65.52%; and NPV 68.42%.

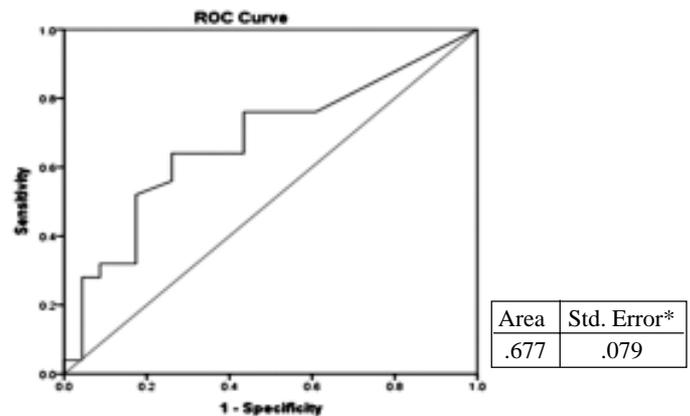


Fig.1: ROC curve and area under ROC curve

Table 4 : Sensitivity and specificity of BALF ADA at various individual values of ADA among the confirmed cases of PTB.

ADA	Sensitivity	Specificity
1.05	0.76	0.63
1.50	0.76	0.61
1.65	0.76	0.61
2.30	0.64	0.43
3.80	0.52	0.27
5.30	0.36	0.17
7.50	0.32	0.08
12	0.28	0.04
19.50	0.20	0.04

DISCUSSION :

Thus this study showed that ADA level was significantly higher in TB patients than in the other two groups (p < 0.05). Pushpakom R et al. in 1988, was the first group reporting higher ADA levels in BALF of tuberculous subjects compared to those from lung carcinoma patients⁶. In a study by Kayacan et al. ADA level in BAL fluids of pulmonary TB patients, non-TB lung disease patients (like interstitial lung disease, lung cancer, pneumonia and COPD) and controls was 3.1±2 IU/L,

0.4±0.5 IU/L and 0.2±0.4 IU/L, respectively (p<0.001)⁷. Another study by Orphanidou et al. compared ADA activity and lysozyme levels in BAL fluid of smear-negative pulmonary TB patients and non-TB lung disease patients and found that there was no significant difference in lysozyme level of BAL fluids between the two groups but ADA level in BAL fluids of pulmonary TB patients was significantly higher than that of non-TB lung disease patients (p<0.001)⁸. In a study conducted by Kubota et al., mean ADA level in BAL fluid of patients with miliary TB, sarcoidosis, idiopathic interstitial pneumonia and control group was 5.02±3.75 IU/L, 1.06±0.99IU/L, 0.21±0.43 IU/L and 0.3±0.51 IU/L, respectively, and ADA level in BAL fluid of miliary TB patients was higher than that of other groups(p<0.01)⁹. An Iranian study by Abolhassan Halvani et.al found a significantly higher levels of BALF ADA in sputum smear negative Pulmonary tuberculosis patients than in other non tubercular lung diseases(p=0.00)¹⁰. However, Reechaipichitkul et al. compared ADA levels in BAL fluid of pulmonary TB patients, lung cancer patients and those with other forms of pulmonary diseases and found no significant difference among these three groups(p=0.56)¹¹. The study by Albera C¹², et al in 1993 and Stratakos G¹³, et al in 1999 showed no significant difference of BALF-ADA between tuberculosis and sarcoidosis groups. This may be due to the same source of ADA production. Furthermore, ADA activity assessed in pleural and peritoneal fluids and CSF had different diagnostic values. ADA values in pulmonary as well as extrapulmonary tuberculosis seemed to vary according to the prevalence of TB in that particular region. ADA levels were found to be high and thus useful in high prevalence countries than in low prevalence countries¹⁴. This is also true about ADA level in BAL fluid. It seems that this laboratory assessment is remarkably dependent on the method of measurement, materials and location. The sample size of this study was not very large and the values were found to be dispersed over a wide range. Furthermore, most studies are on the total ADA level, but ADA isoenzymes would have been more accurate. This study was unable to determine ADA isoenzymes.

CONCLUSION :

Thus, this study showed significantly raised ADA level in bronchoalveolar lavage fluid in sputum smears negative

PTB. This test can be quite useful for diagnosis of sputum smear negative pulmonary tuberculosis especially in high prevalence countries like India. In this study, the mean ADA level was found to be higher in the PTB group, and it is a rapid and cost effective method, but the sensitivity and specificity of the test is low. This may be due to the smaller size of the sample. Therefore, studies with a larger sample size are recommended.

Abbreviations: TB= Tuberculosis, BAL = bronchial veolar lavage, HIV= Human immunodeficiency virus, ADA=adenosine deaminase, IFN-5 γ P= interferon gamma.

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Anaerobic Pleuro – Pulmonary Infections : Is Routine Culture Necessary?

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Abstract

Background: Anaerobes play a major role in pleuropulmonary infections. Obligate anaerobes are the predominant constituents of normal oropharyngeal flora and produce pleuropulmonary infection in patients who are prone to aspirate. Predisposing conditions include prominent dental disease, chronic upper respiratory tract infections and reduced consciousness. **Aims:** To isolate both aerobic and obligate anaerobic bacteria implicated for causing pleuro – pulmonary infections and to evaluate the necessity of routine anaerobic culture for such infection. **Settings and Designs:** A prospective study was conducted over a period of one year. **Methods:** Specimens of pleural fluid, empyema fluid, and aspirates from lung abscess, collected through transthoracic route. Blood was collected from 55 patients, clinically suspected to have pleuro-pulmonary infections. Specimens were processed for isolation of both aerobes / facultative anaerobes and obligate anaerobes using standard microbiological techniques. **Results and Observation:** Out of the 55 cases included in the study, 18 (32.7%) cases showed growth of aerobic organisms while 2 (3.63%) cases showed the growth of anaerobic organisms, the rest being culture negative. From the culture positive cases, the most commonly isolated aerobe was *Klebsiella pneumoniae* (36.84%), followed by *Staphylococcus aureus* (21.05%), *Pseudomonas* spp. (15.78%), *Streptococcus pneumoniae* (10.52%), *Escherichia coli* (5.26%) and *Proteus vulgaris* (5.26%). *Prevotella* spp. was the only anaerobe isolated from 10.52% of the culture positive cases. Blood cultures revealed no growth of any organisms. **Conclusion:** To obtain proper clinical specimens for anaerobic culture is very difficult and also the process of culturing these organisms is very expensive and time consuming. Suspected anaerobic infections can be treated with empirical antibiotics guided by published studies. Therefore routine culture and susceptibility testing for such infection is rarely warranted.

Key words : anaerobes, pleuro – pulmonary infections

INTRODUCTION:

Anaerobic bacteria have been implicated in aspiration pneumonia and its sequelae, including lung abscess, necrotizing pneumonia and empyema since the early 1900s¹. Obligate anaerobes are the predominant constituents of normal oropharyngeal flora and produce pleuro – pulmonary infection in patients who are prone to aspirate². Predisposing conditions include prominent dental diseases, chronic upper respiratory tract infections and reduced consciousness³.

It has also been found that the aetiology of pleuro-pulmonary infections depends on the geographic region, patient's age and advances in the diagnosis and treatment of the underlying cause^{4,5}.

Anaerobic bacteria play a relatively well confirmed

role in selected types of pulmonary infections that are uncommon but distinctive, with common clinical features that include indolent course, putrid discharge and response to antibiotics directed at anaerobes including clindamycin or β -lactam – β -lactamase inhibitors that are favoured for most cases of lung abscess¹.

The clues to the subset that do involve anaerobes include probable aspiration as evidenced by dysphagia (inability to drink water rapidly) or reduced consciousness along with infection in a dependent pulmonary segment with aspiration in the recumbent position or basilar segments with aspiration in the upright position; putrid discharge (sputum, empyema fluid), diagnostic of anaerobes; indolent course (nonspecific); necrosis of tissue with necrotizing pneumonia, lung abscess or empyema with a bronchopleural fistula¹.

Most cases of pneumonia probably do not involve anaerobic bacteria. In addition, the antimicrobials that are commonly used for community acquired pneumonia and other common lung infections like β -lactams, macrolides and flouroquinolones have sufficient activity versus upper airway anaerobes¹.

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Obtaining material from these patients for culture from the site of infection that is uncontaminated by normal flora is problematic. In vitro cultivation of obligate anaerobes requires rigorous anaerobic techniques and susceptibility testing of obligate anaerobes is not standardized in many clinical microbiology laboratories. Few clinical trials of drugs have been done in patients with laboratory documented or putative anaerobic pulmonary infection. For these reasons the diagnosis and therapy of anaerobic pulmonary infection are frequently empirical and guided by published studies of in vitro activity against collected clinical isolates¹.

Considering the above, the present work was undertaken to isolate and identify the bacterial agents causing pleuro - pulmonary infections and to evaluate whether it is actually required to carry out anaerobic cultures on a routine basis in order to manage such infections.

MATERIALS AND METHODS:

The study involved 55 patients suspected to have anaerobic pleuro – pulmonary infections and was done in a tertiary care hospital in Assam, India.

Two specimens of pleural fluid, empyema fluid or aspirates from lung abscess were taken from each patient who had the predisposing factors that might lead to anaerobic pleuro – pulmonary infections. The specimens were collected either transthoracically or intraoperatively.

Gram stains of all the specimens were made and processed following the standard microbiological techniques for isolation and identification of both aerobic and anaerobic organisms^{6,7}.

For isolation of anaerobic organisms, ready to use Thioglycollate broth from Hi Media Laboratories Pvt. Ltd. Mumbai was used as a media for collection and transport of the specimens. The specimens were collected in sterile syringes and inoculated immediately to the pre reduced thioglycollate broth avoiding introduction of any air. Then the broth was incubated anaerobically for 48 hours at 37⁰ C. Then the broth was subcultured on anaerobic blood agar media and incubated in an anaerobic jar at 37⁰ C for 48 hours. Anaerobiasis was achieved by anaerobic gas packs commercially available from Hi Media Laboratories Pvt. Ltd. Mumbai. The organisms isolated anaerobically was further subcultured on blood agar, MacConkey agar

and anaerobic blood agar media and incubated in aerobic and anaerobic conditions respectively to deduce whether the isolate is facultative or obligate anaerobe. Obligate anaerobes showed no growth in plates incubated aerobically and facultative anaerobes were found to be grown in both aerobic and anaerobic conditions. Identification of anaerobic organisms was done manually according to standard guidelines.

For isolation of aerobic organisms, the specimens were collected in a sterile tube. Gram stains were prepared from all the specimens and were inoculated on blood agar and MacConkey agar media. Isolated organisms were identified manually according to the standard guidelines⁷.

Two specimens of blood were taken from all the patients and were processed for isolation of aerobic, facultative anaerobic and obligate anaerobic bacteria.

Isolates of *Staphylococcus aureus* were screened for MRSA using standard guidelines.

All the isolated bacteria were tested against different antimicrobial agents by standard disc diffusion method (Kirby Bauer Technique).

RESULTS:

Out of the 55 cases included in the study, 18 (32.7%) cases showed growth of aerobic organisms while 2 (3.63%) cases showed the growth of anaerobic organisms, the rest being culture negative. (Table1)

Table1: Culture results of the specimens of the 55 cases included in the study

Type of Isolates	No.	Percentage
Only aerobes	17	89.48%
Only anaerobes	1	5.26%
Both aerobes and anaerobes	1	5.26%
Total	19	100%

Table2: Various bacterial isolates of the culture positive cases

Aerobic isolates	
1. Gram negative bacilli	No. (%)
<i>Klebsiella spp</i>	7 (35%)
<i>Pseudomonas spp</i>	3 (15%)
<i>Escherichia coli</i>	1 (5%)
<i>Proteus vulgaris</i>	1 (5%)
2. Gram Positive cocci	No. (%)
<i>Staphylococcus aureus</i>	4 (20%)
<i>Streptococcus pneumoniae</i>	2 (10%)
Total aerobic isolates	18 (90%)
Anaerobic isolates	
Gram negative bacilli	No. (%)
<i>Prevotella spp.</i>	2 (10%)
Total no. of isolates	20 (100%)

Of the four isolates of *Staphylococcus aureus*, two were found to be MRSA.

Of the enterobacteriaceae group, the organisms showed maximum sensitivity to Imipenem (100%), followed by Cefotaxime (77.77%), Piperacillin – Tazobactam and Gentamicin (66.66%), Ciprofloxacin (55.55%), Cefepime (33.33%) and Cefuroxime (22.22%). All the organisms showed resistance to Ampicillin.

The isolated *Pseudomonas* spp showed maximum (100%) sensitivity to Imipenem and Polymyxin B, followed by Amikacin, Tobramycin and Ceftazidime (66.66% each) while Piperacillin – Tazobactam and Ciprofloxacin shows 33.33% sensitivity. None of the *Pseudomonas* isolate was sensitive to Aztreonam.

The Staphylococcal isolates showed maximum (100%) sensitivity to vancomycin and Linezolid, followed by Amoxycylav, Erythromycin and Doxycyclin (50% each) while Gentamicin and Ciprofloxacin showed 25% sensitivity. All isolates were resistant to Penicillin.

Both the isolates of *Streptococcus pneumoniae* were sensitive to Penicillin, Gentamicin, Vancomycin and Linezolid, while one isolate was found to be sensitive to Amoxycylav.

The two isolates of *Prevotella* spp. were sensitive Clindamycin, Piperacillin-Tazobactam, Cefotaxime and Imipenem while only one isolate was found to be sensitive to Cefuroxime and Ciprofloxacin. Both the isolates were resistant to Metronidazole and Ceftriaxone.

Blood culture was done from all the 55 cases included in the study, but none of the cases revealed growth of any organisms.

DISCUSSION:

Out of the 55 cases included in the study, 18 (32.7%) cases showed growth of aerobic organisms while 2 (3.63%) cases showed the growth of anaerobic organisms, the rest being culture negative. Similarly S. Tareen et al¹ found 26% cases to be culture positive and could not recover any anaerobic organism, K. Wanjari⁸ also found only 11.16% of the cases to be culture positive and could not recover any anaerobic organism.

But in comparison to some other studies,^{9, 10, 11, 12, 13} the present study reveals lower isolation rate of anaerobic organisms. This might be due to administration of empirical

antibiotics that are commonly instituted in such patients to stabilize or probably there may not be common involvement of anaerobic bacteria as the etiological agent in such infections in this region of the world as involvement of anaerobes may have a geographical distribution as reported by some studies^{4,5}.

In our study, it was found that amongst the culture positive cases, the most commonly isolated aerobic organism was *Klebsiella pneumoniae* (36.84%), followed by *Staphylococcus aureus* (21.05%), *Pseudomonas* spp. (15.78%), *Streptococcus pneumoniae* (10.52%), *Escherichia coli* (5.26%) and *Proteus vulgaris* (5.26%). *Prevotella* spp. was the only anaerobic organism isolated from 10.52% of the cases. Such findings were also reported by K. Y. Chen et al⁹ and Jiun – Ling Wang et al¹⁴ who reported *Klebsiella pneumoniae* to be the most commonly isolated organism. D. Panigrahi et al¹⁵ also found *Klebsiella pneumoniae* as one of the predominant aerobic pathogen and *Prevotella* spp as the commonest anaerobic isolate.

Blood culture was done from all the 55 cases included in the study, but none of the cases revealed growth of any organism. Such findings were also reported by I. Yaacob and Z. Ariffin¹⁶ who failed to grow any organism from blood culture in 7 out of 13 patients with empyema and could recover *Streptococcus viridans* from only one case out of 9 cases of lung abscess. But J.L. Wang et al¹⁴ reported 18% positive blood cultures in patients with lung abscess.

The negative result for blood cultures in the present study may be attributed due to early administration of antibiotics; moreover the sensitivity of blood cultures can be increased by proper timing of specimen collection and increasing the number of specimens.

Few of the aerobic bacterial isolates were found to be resistant to third and fourth generation Cephalosporins. However all the isolates were sensitive to Carbapenems. Both the anaerobic isolates though sensitive to most of the antibiotics were resistant to Metronidazole.

According to the published guidelines, for community acquired infections, the recommended antibiotics include intravenous amoxicillin – clavulanic acid or a combination of a second generation cephalosporin (e.g. cefuroxime) or clindamycin if the patient is allergic to penicillin and metronidazole¹⁷.

Patients with nosocomial infections need adequate Gram negative coverage as Gram negative organisms are more common in nosocomial infections. For these cases coverage should include at least a carbapenem or antipseudomonal penicillin (e.g. piperacillin – tazobactam) or third or fourth generation cephalosporins (e.g. ceftazidime, cefepime) with metronidazole. If there is a strong suspicion of MRSA coinfection, vancomycin or linezolid can be added. Aminoglycosides should be avoided as these may be inactivated at low pleural fluid p^H and are ineffective against anaerobes¹⁷.

CONCLUSION:

Microorganisms that constitute the normal oropharyngeal flora may gain access to the deeper lung tissues in individuals prone to aspirate. Oropharyngeal secretions are loaded with both aerobic and anaerobic organisms in high concentrations, therefore in an already diseased lung or in generalised immunosuppression, these organisms might overcome the defence mechanism and establish infection.

Different studies have reported that anaerobic organisms are causal factors of various types of pleuro – pulmonary infections. In the current study also two anaerobic organisms were isolated.

But routine culture of anaerobic organisms is a time consuming and expensive task. Collection of appropriate samples and their transport to the laboratory is also very meticulous and must be done properly for successful isolation of anaerobes. Moreover susceptibility testing of anaerobic organisms is not standardized. Considering the above facts it is very difficult to carry out anaerobic culture in a routine basis.

The recommended treatment for anaerobic pleuro – pulmonary infections is surgical intervention and antibiotic administration as early as possible. As culture and antibiotic susceptibility of anaerobes takes a lot of time, it always becomes necessary to start empirical antibiotic administration in order to contain such infection.

As recommended by many other published reports^{2,18} authors of this study would also like to conclude that routine culture and susceptibility testing of anaerobic organisms is not warranted. But studies on anaerobic

isolates of pleura – pulmonary infection should be carried out so as to keep track on the changing trend of anaerobic isolates as causative agents of such infections and their susceptibility pattern.

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Prevalence of asthma and allergic rhinitis among school going children (6-14 years) in Kamrup district, Metro, Assam, India

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Abstract

Background: Asthma and allergic rhinitis prevalence among children is variable among different population. This study was done to evaluate the prevalence of bronchial asthma and allergic rhinitis among school going children in Kamrup district, Assam. Study was conducted over a 15 month period among school going children of the age of 6-14 years. **Methods and Material :** After going through inclusion criteria and exclusion criteria cases were selected for study. An inclusion criterion includes age 6- 14 year, both males and females and willing to participate in the study. An exclusion criterion includes children with active or previous tubercular disease of lung. The selections of schools were done on random basis. Children were assessed by predesigned and pretested Proforma both in English and local language. **Results :** A total of 6010 students from age group of 6 to 14 years were included in the study from 47 schools. Out of 6010, 1007 (16.75%) belongs to rural and 5003 (83.25%) belongs to urban area. The rural and urban prevalence of asthma symptoms was 11.9% and 10% respectively. Out of 6010 children, 453 (7.5%) children had family history of asthma and 1089 (18.1%) had family history of allergic rhinitis. In our study we found that 1343 (22.3%) had frequent running nose and sneezing, 1473 (24.5%) had nasal blockage and 1111 (18.5%) had history of limitation in activity due to nasal symptoms. **Conclusions :** The study found prevalence of asthma similar to some studies conducted in other parts of India but there is variation with other studies. However the prevalence of allergic rhinitis was higher compared to national data. This variation of prevalence of asthma and allergic rhinitis in different parts of India may have several factors including but may not be limited to tools used for evaluation, environment, pollution, pollen, culture, behaviour, availability of medical service, urbanization, education and awareness etc from place to place.

Keywords : asthma prevalence, allergic rhinitis

INTRODUCTION :

Asthma and allergic diseases are common among children. Asthma is a chronic disease of airways and its prevalence varies from countries to countries and from regions to region within the country¹. This variable in prevalence may be due to several factors. Prevalence is higher in western European countries than eastern European and developing countries². International Study of Asthma and Allergies in Childhood (ISSAC) and some other studies have been reported low prevalence rates (2%–4%) in Asian countries, Eastern European, Indonesia, Greece etc. and high prevalence rates (15%–20%) in the United Kingdom, Canada, Australia, New Zealand, Ireland, North, Central and South American countries^{1,2,3,4,5}. In India also this variation has been observed. Prevalence of asthma has been reported in

various studies from 0.2 to 15%⁶. ISSAC study found low prevalence of asthma in Lucknow, Ludhiana and Punjab (1-3.3%)². In Delhi the recorded prevalence was 11.6%⁷. Bangalore recorded an increase in prevalence of bronchial asthma from 9 to 29.5% during period of 1979 to 1999 which is the highest recorded prevalence in India⁸. Variable prevalence of allergic rhinitis has also been reported in various studies^{2,9}. The rate of urbanization, environment, education and awareness may be some of the factor which may affect the variability of asthma prevalence from countries to countries and from regions with in the country.

SUBJECTS AND METHODS :

The present study on “prevalence of bronchial asthma among school going children in Kamrup district metro (both rural and urban)” was conducted over a 15 month period by the Department of Pulmonary Medicine, Gauhati Medical College, Guwahati, Assam among school going children of the age of 6 to 14 years after institution ethical committee clearance. It was a cross sectional study and was done in Kamrup district metro, both urban and rural

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areas. It is mentioned that undivided Kamrup district is made into two districts, Kamrup and Kamrup Metro which mostly comprises of Gauhati Municipal Corporation area and Kamrup Metro also comprise rural and urban area. The cases were taken from different Lower Primary (LP) and Middle English (ME) schools of Kamrup Metro by simple random assessment. The data collection was done for 12 months and for analysis and computer work it took another 3 months.

Inclusion criteria

1. Age 6- 14 year, both males and females
2. Willing to participate in the study

Exclusion criteria

1. Children with active or previous tubercular disease of lung based on history and previous medical records
2. <6 and >14 years

Baseline assessment

The selection of schools were done on random basis on different parts of district after taking permission from District Education Department and then from Headmaster/ Headmistress of the respective schools and approval from Institutional Ethical Committee. Students were included who were cooperative and gave consent to participate in the study by themselves or by parents. Diagnosis of asthma and allergic rhinitis was diagnosed based on criteria as mentioned by GINA and ARIA guidelines respectively.. The observations of the cases were analyzed manually and presented in tabular form. Statistical analysis was done using SPSS 15.

RESULTS :

According to 2011 census In Kamrup district Metro total population is 1,260,419 of which male and female were 655,630 and 604,789 respectively. Out of total population 17.10% live in rural area and 82.90% in urban area. Total 47 schools were visited (39 in urban and 8 in rural area). Out of 47 schools 34 schools were coeducation, 9 were girls' school and 4 were boy's school.

A total of 6010 students from age group of 6 to 14 years old from Kamrup Metro district were included in the study during the period from August 2011 to August 2012. Proforma was filled up with the help of parent. Students were from different LP and ME schools. Out of 6010, 1007 (16.75%) belongs to rural and 5003 (83.25%) belongs to urban area. Age of the children range

from 6 to 14 years, mean age 11.88 ± 1.87 years. Average age of male children was 11.84 years and female children were 11.92 years. Out of 6010, 3312 (55.1%) were female and 2698 (44.9%) were male.

Table 1 : demographic profile of the study population

Demographic profile of study population		
Age		Range 6-14 year Mean $11.88 \pm SD 1.87$
Sex	Male	2698 (44.9%)
	Female	3312 (55.1%)
	Rural	1007 (16.75%)
	Urban	5003 (83.25%)

Table 2 : Frequency of male and female students in relation to Urban and Rural areas.

Area	Male	Female	Total
Urban	2185	2818	5003 (83.25%)
Rural	513	494	1007 (16.75%)
Total	2698 (44.9%)	3312 (55.1%)	6010

Children were evaluated for family history and symptoms of asthma and allergic rhinitis. The data showed that out of 6010 children, 453 (7.5%) children had family history of asthma and 1089 (18.1%) had family history of allergic rhinitis.

Table 3 : showing frequency of family history of asthma and allergic rhinitis

	Total	%
Family history of asthma	453	7.5%
Family history of allergic rhinitis	1089	18.1%

Children were analysed for symptoms related to asthma and allergic rhinitis. Out of 6010 children 295 (5%) had recurrent attack of wheezing, 625 (10.4%) had trouble some cough at night, 110 (1.8%) had shortness of breath, wheezing or coughing after exercise, 105 (1.75%) had wheezing, chest tightness or coughing after exposure to air-born allergen or pollutant, 1343 (22.3%) had frequent running nose and sneezing, 1473 (24.5%) had nasal blockage and 1111 (18.5%) had history of limitation in activity due to nasal symptoms. 257 (4.3%) had history of self reported asthma and 384 (6.39%) had history of asthma medication use. The overall asthma symptoms were found among 10.4% children and allergic rhinitis symptoms in 24.5% children. The asthma symptoms among rural population were 11.9% and allergic rhinitis symptoms was 21.9%, whereas in urban population the asthma symptoms were 10% and allergic rhinitis symptoms was 25.1% among children.

Out of 6010 students 61% father had the history of

Table 4 : Frequency of symptoms along with rural and urban prevalence

Symptoms in last 12 month	frequency	Rural 1007 (% rural prevalence)	Urban 5003 (% urban prevalence)	Overall prevalence %
Recurrent attack of wheezing	295	53 (5.2%)	242 (4.8%)	5
Troublesome cough at night	625	120 (11.9%)	505 (10%)	10.4
Shortness of breath/ wheezing or coughing after exercise	110	11 (1%)	99 (2%)	1.8
Wheezing, chest tightness or coughing after exposure to air-born allergen or pollutant	105	10 (0.9%)	95 (1.9%)	1.75
Frequent running nose and sneezing	1343	221 (21.9%)	1122 (22.4%)	22.3
Nasal blockage	1473	218 (21.6%)	1255 (25.1%)	24.5
Limitation in activity due to nasal symptoms	1111	187 (18.6%)	924 (18.5%)	18.5

smoking and 39% had no history of smoking. When we compared history of asthma in relation to smoking history of father we found that out of 3668 of children whose father used to smoke, 241 (6.57%) children had history of bronchial asthma whereas out of 2342 children whose father were non smoker 143 (6.12%) had history of bronchial asthma. Although there is more number of children whose father used to smoke have history of asthma as compared to non smoker father but it was not statistically significant ($p > .05$).

Table 6 : Comparison of bronchial asthma in relation to smoking in presence of children.

Smoking in presence of children	bronchial asthma
Yes 2063	138 (6.69%)
No 1605	103 (6.42%)
3668	241

When we compared history of asthma in relation to smoking history of father in presence of children we found that out of 3668 father, 2063 father used to smoke in the presence of children. Among them 138 (6.69%) had history of bronchial asthma where as out of 1605 father, who do not smoke in presence of children, 103 (6.42%) children had history of bronchial asthma. Although the number of children whose father smoke in their presence had history of asthma symptoms but it is statistically insignificant.

Table 5 : Comparison of bronchial asthma in relation to smoking history of father

Smoking history of father	Bronchial asthma of children
Yes 3668	241 (6.57%)
No 2342	143 (6.12%)
6010	384

DISCUSSION :

Prevalence of asthma and allergic disorders are variable from country to country and also within the country. India is a vast country with different regions having different socio-cultural environments and variant climatic pattern. Our study which evaluated the prevalence of asthma and allergic disorders among school children with a sample size of 6010 has found asthma symptoms among 10.4% children. The rural and urban prevalence of asthma symptoms was 11.9% and 10% respectively. Although there is more prevalence of asthma symptoms among rural area but it is statistically insignificant. In other studies the prevalence was variable in different parts of the country. The initial study done in 1966 showed prevalence of asthma in children <9 years age to be only 0.2%¹⁰. Chhabra et al in 1998 showed that in children of Delhi the current prevalence of asthma 11.6%⁷. Awasthi et al showed that in Lucknow the prevalence of asthma was 2.3 % and 3.3% among 6-7 year and 13-14 years age group respectively¹¹. In Shimla 1186 children were included in a questionnaire based study with response rate of 89.5% showed the overall prevalence of asthma to be 2.3%¹². In a multi centric study in India asthma was diagnosed in 2.28%, 1.69%, 2.05% and 3.47% respondents respectively at Chandigarh, Delhi, Kanpur and Bangalore, with overall prevalence of 2.38%¹³. Singh et al in their study with 2275 children from 1-15 years age group in Ludhiana found that the prevalence of chronic/ recurrent cough was 1.06%¹⁴. In rural population in South India with a total sample of 555 the prevalence of bronchial asthma was found to be 10.3%¹⁵. In another study from rural Puducherry, located in South India the overall prevalence of bronchial asthma was found to be 8.7% where sample size was 275¹⁶. Narayana et al carried out a study in rural areas of Dakshina Kannada District of Karnataka state in India and found that the prevalence of ever wheezers is 8.4% and current wheezers is 5.2%¹⁷.

In our study we found that 1343 (22.3%) had frequent running nose and sneezing, 1473 (24.5%) had nasal blockage and 1111 (18.5%) had history of limitation in activity due to nasal symptoms. In India, ISSAC phase I study was conducted in 14 centres and nasal symptoms alone were present in 12.5% children in the 6-7 years age group and 18.6 % in the 13- 14 years age group⁹. In the International Study of Asthma and Allergies in Childhood

(ISAAC) Phase III the global prevalence of current rhinoconjunctivitis symptoms was 14.6% for the 13- to 14-years old children¹⁸. Gaur et al in their study included 5900 subjects and found the prevalence of allergic rhinitis 11.69% among adolescents and adult population in Delhi¹⁹. In our study we found higher prevalence of allergic rhinitis symptoms than the average national data. We also analysed the relation of parental smoking and asthma. There is higher number of children have asthma whose parent used to smoke but it did not meet statically significance. Kumar et al also did not found significant relation between asthma and parental smoking¹⁶.

This variation of prevalence of asthma and allergic rhinitis in different parts of India may have several factors. There is variation in term of tools used, environment, pollution, pollen, culture, behaviour, availability of medical service, urbanization, education and awareness etc from place to place. These factors need to be evaluated to know this epidemiological variation and which may guide future research in asthma. This variable prevalence may affect treatment outcome as well.

Key Messages : *The finding of variable prevalence of asthma and allergic rhinitis indicated the association of factors whose evaluation may impact treatment outcome.*

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Diphtheria – An Overview

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INTRODUCTION :

Diphtheria is a disease caused by the bacteria *Corynebacterium diphtheriae*, some strains of *C.ulcerans* and very rarely *C. pseudotuberculosis*, may produce diphtheria toxins and the illness caused may present as clinical diphtheria, it can cause respiratory symptoms and non- respiratory symptoms. The word diphtheria originates from the term *diphtherite* which has a greek root meaning (skin or hide) and refers to the leathery appearance of the characteristic pharyngeal membrane.¹ Diphtheria has declined dramatically over the past 80 years but it remains an important disease in many parts of the tropics and there has been a recent resurgence of the disease in the West between 1990 and 1999 over 1,58,000 cases and 4,000 deaths were reported in the country's of the former Soviet union since 2002. *C.ulcerans* has been more commonly reported than *C. diphtheriae* in the UK and France, infections are usually acquired from raw milk and contacts with farms and farm animals and pets.¹The increasing incidence in the illness has resulted in expansion of the notification criteria of the E-CDC and US- CDC for diphtheria to include infections caused by *C.diphtheria* and *C.ulcerans* the increase in the number of clinical cases of diphtheria also highlights the need to maintain the vaccination coverage in the population above 95% as recommended by WHO.

EPIDEMIOLOGY:

The only reservoir of *C.diphtheriae* is the human. Diphtheria spreads from person to person either from acute cases or from asymptomatic carriers. The principal modes of spread are by respiratory droplets or direct contact with the secretions of respiratory tract or exudates from

infected skin. Epidemics have been caused by milk contaminated by human carrier. Some patients become carriers and continue to harbor *C. diphtheriae* for weeks to months.²The incidence of diphtheria in Western world has decreased in the last 50-75 years(152cases per 1,00,000 population in 1920 to 0.002 per 1,00,000 in 1980 in the USA). In 2008, 47 cases were reported across the EU. Therefore, high vaccination coverage must be maintained, adult booster coverage increased, and epidemiological surveillance and laboratory capacity preserved despite of small number of cases.

Indian Scenario : Diphtheria is an endemic disease, the available retrospective data indicate a declining trend of diphtheria in the country. It is due to increasing coverage of child population by immunization, The reported incidence of the disease in country in 1987 was about 12,952, in 2008 India contributed to 6,081 cases of Diphtheria whereas during the year 2009 there was 3,480 cases and 113 deaths showing a case fatality rate of about 3.25.

Scenario in Assam: There were no reports of outbreaks of Diphtheria in Assam in the last few years, though sporadic cases were reported. The number of cases coming to Assam Medical College & Hospital Dibrugarh, were very few and immunization coverage in Assam was 19.30% (2006) which was improved to 67.60% in 2007. In Dibrugarh District of Assam in 2008-09 immunization coverage was 90%. A total of 60 cases was reported Barbaruah Block of Dibrugarh in 2010. Majority cases belonged to 20-44 years and of the 60 cases investigation was done in 44 cases and Lab. Confirmed cases were eight in number.³

Agent Factor :

a) AGENT: The causative agent , *C. diphtheria* is gram positive , non-motile organism. It has no invasive power but produces a powerful exo-toxin. Four types of

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diphtheria bacilli are differentiated- *gravis*, *mitis*, *belfanti* and *intermedius*, all pathogenic to man, in general *gravis* infection tends to be more infectious than *mitis* infections.⁴

b) Source of Infection : *The source of infection may be case or carrier.*

CASE : *Case ranges from subclinical to frank clinical cases. Mild or silent infections may exhibit no more than a mere running nose or sore throat; this can play a more important role than frank cases in spreading the infections.*

CARRIER : *Carriers are common source of infections, their ratio is estimated to be 95 carriers for 5 clinical cases, carrier may be temporary or chronic; nasal or throat carriers, the nasal carriers are particularly dangerous as source of infections because of frequent shedding of the organism into the environment, than do throat carriers. The temporary carrier state may last for about a month, but the chronic carrier state may persist for years or so, unless the patient is treated. The incidence of carriers in a community may vary from 0.1 to 5 percent . Immunization does not prevent the carrier state.*

c) INFECTIVE MATERIAL: *Nasopharyngeal secretions, discharge from skin lesions, contaminated fomites, and possibly infected dust.*

d) PERIOD OF INFECTIVITY: *Unless treated, the period of infectivity may vary from 14 to 28 days from the onset of the disease but carriers may remain infective for much longer period .*

A case or carrier may be considered non communicable, when at least 2 cultures properly obtained from nose and throat , 24 hours apart , are negative for diphtheria bacilli.

HOST FACTORS :

- a) Age : Diphtheria particularly affects children aged 1 to 5.
- b) Sex : both sexes are affected .
- c) Immunity : infant born of immune mothers are relatively immune during the first few weeks or months of life. A herd immunity of over 70% is considered necessary to prevent epidemic spread, but some believe that the critical level may be as high as 90%.

ENVIRONMENTAL FACTORS :

Cases of diphtheria occur in all seasons, although

winter months favour its spread. In Kolkata , the highest incidence was reported in August ; in Mumbai in the winter months, in New Delhi during August to October .

MODE OF TRANSMISSION :

The disease is spread mainly by droplet infection. It can also be transmitted directly to susceptible persons from infected cutaneous lesions. Transmission by objects (e.g cups, thermometers, toys, pencils), contaminated by the nasopharyngeal secretions of the patient is possible, but for only short periods.

PORTAL OF ENTRY :

a) Respiratory Route: Commonly the portal of entry is the respiratory tract.

b) Non Respiratory Routes: The portal of entry some times, may be the skin where cuts , wounds and ulcers are not properly attended to , may get infected with diphtheria bacilli, and so is the umbilicus in the newborn . Occasionally, the site of implantation may be the eye, genitalia or middle ear.

INCUBATION PERIOD : 2 to 6 days, occasionally longer.

The only reservoir of *C.diphtheriae* is the human. Diphtheria spreads from person to person either from acute cases or from asymptomatic carriers. The principal modes of spread are by respiratory droplets, direct contact with the secretions of respiratory tract or exudates from infected skin. Epidemics have been caused by milk contaminated by human carrier.

High vaccination coverage must be maintained, *adult booster* coverage increased, and epidemiological surveillance and laboratory capacity preserved .

PATHOGENESIS :

The potentially lethal effects of diphtheria in humans are caused by an exotoxin. The toxigenicity of *C. diphtheriae* depends on the presence of a tox phage alpha lysogenic beta phase. Diphtheria toxin is a 6200 Da polypeptide which includes two segments – theta active toxin moiety A and the binding B augment, which binds to specific receptors on susceptible cells. The diphtheria toxin effects all human cells, but the most profound effects are on the myocardium (myocarditis), peripheral nerves (demyelination) and kidneys (acute tubular necrosis).

CLINICAL MANIFESTATION

Three major clinical types – anterior nasal, faucial and laryngeal have been described. However, skin, conjunctiva, genitals and other parts of the body may be affected.



Nasal Diphtheria



Pharyngeal Diphtheria



Cutaneous Diphtheria



Bull's Neck



Corneal Diphtheria



Diphtheria of Male Genital Tract

CASE DEFINITION

Clinical Description : An illness characterized by laryngitis, pharyngitis or tonsillitis and an adherent membrane of tonsils, pharynx or nose.

Lab Criteria for Diagnosis : Isolation of *Corynebacterium diphtheriae* from a clinical specimen or a four-fold or greater rise in serum antibody but only if both serum samples are obtained before administration of diphtheria toxoid or anti- toxin.

CASE CLASSIFICATION :

- a) **Probable** – A case that meets the clinical description.
- b) **Confirmed** – A probable case that is laboratory confirmed or linked epidemiologically to a lab confirmed case. Clinical manifestations appear after an incubation period of 1-6 days and depends on the site of infection, host immunity and whether the toxin has entered the systemic circulation.

Differential Diagnosis

- i) Streptococcal/ Viral pharyngitis and tonsillitis
- ii) Vincent’s angina
- iii) Infectious mononucleosis
- iv) Mumps – in case of a ‘bull neck’ (Malignant diphtheria)

Complications

- a) Respiratory failure
- b) Cardiac- Myocarditis, Cardiac Dilatation and Failure, Mycotic Aneurysm and Endocarditis, Heart Block including AV Dissociation and Dys-arrhythmias
- c) Secondary bacterial pneumonia
- d) Cranial Nerve Dysfunction and Peripheral Neuropathy
- e) Optic Neuritis
- f) Septicemia/ Shock
- g) Septic Arthritis, Osteomyelitis
- h) Metastasis or infection to spleen, myocardium or CNS

DIPHTHERIA MANAGEMENT GUIDELINES

Emergency/Casualty Department Care

Treatment of diphtheria should be initiated even before confirmatory tests are completed due to the high potential for mortality and morbidity. All cases should be isolated promptly and universal and droplet precautions should be used to limit the number of possible contacts. There should be a secure definitive airway for patients with impending respiratory compromise or the presence of laryngeal membrane. Early airway management allows access for mechanical removal of tracheobronchial membranes and prevents the risk of sudden asphyxia through aspiration. Involving ENT or Anaesthesia personnel should be considered for intubation and securing of airway if there is suspicion for loss of the airway or respiratory failure. Close monitoring of cardiac activity should be maintained for early detection of rhythm abnormalities. Electrical pacing should be initiated for clinically significant conduction disturbance and pharmacologic intervention should be

provided for arrhythmias or for heart failure. 2 large-bore IVs must be provided for patients with a toxic appearance; invasive monitoring and aggressive resuscitation must be provided for patients with septicemia. Prompt antibiotic coverage (erythromycin or penicillin) must be initiated for eradication of organisms, thus limiting the amount of toxin production. Antibiotics hasten recovery and prevent the spread of the disease to other individuals. The toxin should be neutralized as soon as diphtheria is suspected. Diphtheria antitoxin is a horse-derived hyper-immune antiserum that neutralizes circulating toxin prior to its entry into the cells. It prevents the progression of symptoms. The dose and route of administration (IV vs IM) are dependent on the severity of the disease. This antitoxin must be obtained directly from the Centers for Disease Control and Prevention (CDC) through an Investigational New Drug (IND) protocol. The patient must be tested for sensitivity to the antitoxin before it is given.

Diphtheria disease does not confer immunity; thus, initiation or completion of immunization with diphtheria toxoid is necessary. Throat and nasal swabs should be obtained from persons in close contact with the suspected diphtheria victim and age-appropriate diphtheria booster should be administered. Antibiotic therapy with erythromycin or penicillin for chemoprophylaxis should be initiated in a patient with suspected exposure. Throat cultures should be repeated in 2 weeks after treatment.

MEDICATION SUMMARY :

Patients with active disease as well as all close contacts should be treated with antibiotics.^{5,6} Treatment is most effective in the early stages of disease and decreases the transmissibility and improves the course of diphtheria. Additionally, close contacts, such as family members, household contacts, and potential carriers, must receive chemoprophylaxis regardless of immunization status or age.⁷

a) This entails treatment with erythromycin or penicillin for 14 days and post treatment cultures to confirm eradication. The CDC has approved macrolides such as erythromycin as first-line agents for patients older than 6 months of age. The horse serum antitoxin is given to anyone suspected to have diphtheria and can be administered without confirmation from cultures, as it is

most efficacious early during the course of the disease.

b) Anti-toxins : Neutralizes the toxins before they enter the cells.⁸ Dose given depends on the site of infection, length of time patient is symptomatic and the severity of illness and extent of pseudo- membrane formation, and the time delay between the onset and the anti-toxin administration.

- 20,000 – 40,000 units for faucial diphtheria of less than 48 hours duration.
- 40,000 – 80,000 units for faucial diphtheria of more than 48 hours duration.
- 80,000 – 100,000 units for malignant diphtheria (bull neck & toxic state)

ANTIBIOTICS :

Erythromycin and penicillin are both recommended for the treatment of diphtheria. Some studies suggest that erythromycin may be better at eradication of the carrier state. Penicillin is recommended in household contacts who may not comply with the duration of erythromycin treatment. It is believed that azithromycin may be a better macrolide treatment in this population. The treatment of endocarditis requires the addition of an aminoglycoside. Erythromycin Dose - Parenteral or Oral 5ml/kg—4 times daily, Penicillin Dose—50,000 units/kg daily in 4 divided doses. Penicillin may be used for treatment, prophylaxis, and eradication of diphtheria in carriers. However, resistant strains and transmission from penicillin-treated carriers has been reported.

Penicillin G benzathine penicillin Interferes with synthesis of cell wall mucopeptides during active multiplication, which results in bactericidal activity. Effective treatment for systemic diphtheria.

Outpatient Care : Age-appropriate immunization schedule should be completed. All household and other close contacts should be treated with antibiotics as mentioned above. All suspected and confirmed carriers should be treated with erythromycin or penicillin for 14 days. Follow-up pharyngeal cultures must be obtained post treatment, confirming eradication of the bacterium.

Inpatient Care: Supportive care should be provided for continuation of antibiotic treatment and antipyretics for fever . Close observation should be made in case of development of primary or secondary bacterial pneumonia. Serial ECGs should be performed

to detect cardiac abnormalities. Physical therapy should be provided for patients with neurologic dysfunction. Patients with endocarditis may require valve replacement, especially with previous prosthetic valves. However, some evidence suggests that antibiotic therapy with a beta-lactam with or without an aminoglycoside may be adequate in treating endocarditis with either a native or prosthetic valve. Respiratory isolation may be indicated. Monitoring should be done for serum sickness or hypersensitivity reactions in patients treated with DAT (Diphtheria Antitoxin)

Inpatient & Outpatient Medications

The following medications may be necessary:

- A) Bronchodilators (may be beneficial for patients with mild respiratory symptoms)
- B) Antipyretics
- C) Antibiotics - Penicillin, erythromycin

Transfer to ICU- Intensive care unit admission is recommended for patients with impending respiratory compromise. Isolation may be indicated.⁹

PREVENTION :

The 4 forms of the diphtheria toxoid are as follows: DTaP, Tdap, DT, and Td.¹⁰ The childhood vaccination is called DTaP. Adult vaccination form is Tdap. These toxoid vaccinations are combined with acellular pertussis and tetanus vaccine. DTaP is given at 2 months, 4 months, 6 months, 15-18 months, and 4-6 years. Td is a vaccine for adolescents and adults given as a booster every 10 years or when an exposure has occurred. Tdap is recommended for adolescents aged 11-12 years or in place of one Td booster in older adolescents and adults aged 19 years and older. In 2012, the CDC recommended patients 65 years and older receive Tdap if they have not received it previously. Boostrix is Tdap approved for adolescents aged 10 years and older, and Adacel is Tdap approved for those aged 11-64 years. For those 65 and older, the CDC recommends Boostrix. However, either Boostrix or Adacel may be used depending on availability. The CDC also recommends that pregnant patients greater than 20 weeks gestation be given Tdap during pregnancy or shortly after delivery. CDC's Advisory Committee for Immunization Practices

recently recommended that pregnant patients greater than 20 weeks' gestation receive Tdap regardless of previous Tdap history. This allows maternal antibodies to pass on to the fetus, giving protection for the few months of life. Therefore, Tdap Boostrix, and Adacel are now recommended in the immunization schedule for prevention of endemics associated with pertussis and diphtheria. Contact/respiratory isolation is indicated for prevention and deterrence of spreading the infection. Adult forms of vaccination are not available worldwide.

Prognosis : Cardiac involvement is associated with a very poor prognosis¹², particularly myocarditis and AV and left bundle-branch blocks (mortality rate 60-90%). Bacteremic disease carries a mortality rate of 30-40%. High mortality rate is seen with invasive disease. High mortality rates are seen in individuals younger than 5 years and in those older than 60 years

CONCLUSION :

Diphtheria is predominantly a disease of childhood. Diphtheria presents in a variety of different forms depending upon the location of the pseudomembrane. The 'GREY-White' membrane is the hallmark of the infection. It is caused by the destructive effects of the toxin on epithelial cells. The membrane is composed of leucocytes, bacteria, cellular debris and fibrin. It is adherent to the underlying tissues and bleeds if pulled away. In clinical practice, the disease can be divided into nasal, faucial, tracheolaryngeal, cutaneous and malignant diphtheria.

Severe/Malignant Diphtheria is a terrible disease¹¹. Even if patients survive the acute destructive phase, they are likely to die from the remote effects of the toxin. Patients recovering from Diphtheria may die suddenly within 8 weeks following the acute disease. The most prominent toxic complications of Diphtheria are myocarditis and neuritis. The risk and the severity of toxin damage correlate with the extent of the pseudomembrane and delay in the administration of anti-toxin. The frequency of Cardiac Involvement following laryngeal and malignant Diphtheria is 3 – 8 folds higher than tonsillar Diphtheria.

Less common complications of Diphtheria include acute tubular necrosis, DIC, endocarditis and secondary pneumonitis. The overall mortality rate of diphtheria is

approximately 5 – 10% with relatively higher rates in infancy and elderly.

In spite of vaccination given under UIP, the disease is still occurring as sporadic cases in India including Assam. The case fatality in admitted cases were very high.

In cases of sorethroat with visible membrane the diagnosis of Diphtheria must be strongly considered and proper prophylactic measures should be taken by the health care providers alongwith isolation and treatment of cases adequately with antibiotics and ADS. Myocarditis is a common mode of complication leading to death in Diphtheria.¹² Early diagnosis and timely intervention can prevent death due to diphtheria.

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Ulcerative Colitis

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INTRODUCTION :

Ulcerative colitis (UC) is a chronic inflammatory disease with continuous colonic mucosal inflammation without granulomas on biopsy, characteristically affecting the rectum and a variable extent of the colon in continuity, which is characterised by a relapsing and remitting course. It usually presents in late adolescence and early adulthood, although the diagnosis may be made at any age. Both sexes are equally affected. Few patients have rectal sparing variant and peri-appendiceal patchy inflammation. Symptoms depend on the extent and severity of disease, extra-intestinal manifestations and concurrent therapy. Enteric pathogens may alter the clinical presentation.

IBD unclassified (IBDU) is the term used when distinction between UC, Crohn's disease, or other cause of colitis cannot be made despite history, endoscopy, histopathology of mucosal biopsies and radiology.

Indeterminate colitis is a term used by pathologists for a colectomy specimen with overlapping features of UC and Crohn's disease. It has distinct prognostic factors related to further surgery.

DISTRIBUTION OF DISEASE :

The Montréal classification (Figure-1) is used for defining the distribution of disease to describe the maximal,

Figure 1 : Distribution of UC

Term	Distribution	Description
E1	Proctitis	Involvement limited to the rectum (i.e. proximal extent of inflammation is distal to the rectosigmoid junction)
E2	Left-sided	involvement limited to the proportion of the colon distal to the splenic flexure (analogous to 'distal' colitis)
E3	Extensive	involvement extends proximal to the splenic flexure, including pancolitis.

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macroscopic extent of disease at colonoscopy. The extent influences the patient's management, treatment modality and surveillance.

DISEASE ONSET :

There is some evidence to suggest that patients with UC stratified by age (**A1: <16; A2:16–40 and A3: >40 years**) have different outcomes. Onset before 16 years of age has a more aggressive initial course, while older age is associated with a lower risk of colectomy.

CLINICAL FEATURES :

The presenting symptom in more than 90% patients is loose stool with visible blood. Extensive UC present with chronic diarrhoea and rectal bleeding associated with urgency, tenesmus, passage of mucopurulent exudates, nocturnal defecation and crampy abdominal pain, or ache over the left iliac fossa prior to and relieved by defecation. Those with proctitis have similar complaints and occasionally severe constipation. Although simple fistulae occasionally occur in UC, recurrent or complex perianal fistulae should raise the suspicion of Crohn's colitis.

UC usually presents insidiously with symptoms persisting for weeks or months before diagnosis. Severe attack occurs in about 15% with systemic symptoms including weight loss, fever and tachycardia. Extraintestinal manifestations like axial or peripheral arthropathy, episcleritis and erythema nodosum occurs in about 10% and rarely precede intestinal symptoms. Thromboembolism is generally associated with active disease and pancolitis.

RISK FACTORS :

Appendectomy for histology proven appendicitis has been shown to provide some protection against subsequently developing UC and in reducing its severity. Non-selective NSAIDs is associated with increased risk for exacerbating UC. Short term use of COX-2 inhibitors

is probably safe. A family history of CD or UC increases the risk for developing UC in another family member.

HISTORY AND EXAMINATION :

Medical history should include onset of symptoms, particularly recurrent episodes of rectal bleeding or bloody diarrhoea, urgency, tenesmus, abdominal pain, incontinence, nocturnal diarrhoea, and features of extra-intestinal manifestations.

Recent travel, food intolerances, contact with enteric infections, medication (including antibiotics and non-steroidal anti-inflammatory drugs), smoking habit, sexual practice, family history of IBD & CRC and previous appendectomy should be explored .

Physical examination should include vitals, weight and height, abdominal distention and tenderness, perianal inspection, digital rectal examination, oral inspection, and check for eye, skin and/or joint involvement. Examination may be unremarkable in mild or even moderate disease.

DIAGNOSIS :

There is no gold standard for the diagnosis of UC. The diagnosis is established by combination of medical history, clinical evaluation, and typical endoscopic and histological findings. An infective cause should be excluded. Where there is doubt endoscopic and histological confirmation is necessary after an interval.

INVESTIGATIONS :

Initial laboratory investigations should include a full blood count, stool examination, serum urea, creatinine, electrolytes, liver enzymes, iron studies, and C-reactive protein (CRP). Faecal calprotectin is an accurate marker of colonic inflammation. CRP and erythrocyte sedimentation rate (ESR) are useful markers to monitor the response to treatment in severe colitis. Microbiological testing for infectious diarrhoea including *Clostridium difficile* toxin is recommended. Immunization status to various viral diseases and tuberculosis status should be assessed.

In established UC, microbial testing is recommended in cases of severe or refractory relapse, including testing for *Clostridium difficile* and Cytomegalovirus. Serological markers like perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA) are found in up to 65% of patients

with UC and in less than 10% of patients with Crohn’s disease. Faecal markers of intestinal inflammation, neutrophil derived proteins such as calprotectin, elastase, lysozyme and lactoferrin, have been evaluated in IBD. Faecal calprotectin appears to be the most sensitive, non-invasive biomarker that reflects intestinal inflammation in established IBD. However, as with all faecal tests, calprotectin lacks the specificity to discriminate between types of inflammation. Therefore, its use as a diagnostic tool in UC is limited, although its value may yet prove to be a marker with high negative predictive value in patients with a low likelihood of other pathology.

For suspected UC, colonoscopy, preferably with ileoscopy, and segmental biopsies including the rectum are the preferred procedures to establish the diagnosis and extent of disease. Patients with a severe attack should have abdominal radiography and active disease confirmed by sigmoidoscopy as a first line procedure.

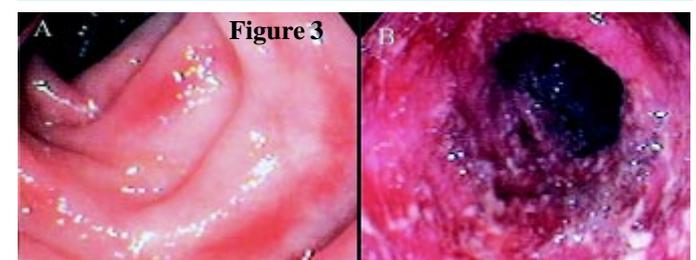
ACTIVITY INDICES IN UC :

Instruments for measuring clinical and/or endoscopic disease activity in UC are available, but none has been adequately validated. In daily routine such indices are rarely used. Immediate admission to hospital is warranted for all patients fulfilling *Truelove and Witts’ criteria* for severe colitis to prevent delayed decision-making which may lead to increased perioperative morbidity and mortality.

Disease activity is grouped into remission, mild, moderate and severe. *Truelove and Witts’ criteria* is used in clinical practice (Figure 2), in conjunction with

Figure 2 : Truelove & Witts disease activity in UC

	Mild	Moderate in between mild and severe	Severe
Bloody stools/day	< 4	4 or more if	≥ 6 and
pulse	<90 bpm	≤ 90 bpm	> 90 bpm or
Temperature	<37.5°C	≤ 37.8°C	> 37.8°C or
Haemoglobin	>11.5 g/dL	≥ 10.5 g/dL	<10.5 g/dL or
ESR	<20 mm/h	≤ 30 mm/h	>30mm/h or
CRP	Normal	≤ 30 mg/L	> 30 mg/L



colonoscopy (Figure 3) to confirm active colitis.

Figure-3 demonstrating colonoscopic findings in mild ulcerative colitis demonstrating edema, loss of vascularity, and patchy subepithelial haemorrhage (A) & severe ulcerative colitis demonstrating loss of vascularity, hemorrhage, and mucopus (B). The mucosa is friable, with spontaneous bleeding as well as bleeding after the mucosa is touched by the endoscope.

Disease severity influences the treatment modality and determines if no, oral, intravenous or surgical therapy is initiated. Severe colitis according to above criteria mandates hospital admission for intensive treatment and defines an outcome (only 70% respond to intensive therapy). The simplest clinical measure to distinguish moderate from mildly active colitis is the presence of *mucosal friability* (mucosal bleeding on sufficient pressure for 3 seconds on the mucosa with closed biopsy forceps to create a dimple).

Histopathology

Multiple (a minimum of two samples) biopsies from five sites (including rectum) and the ileum should be obtained. Basal plasmacytosis at the initial onset has a high predictive value for diagnosing IBD. Repeat biopsies after an interval may help to solve differential diagnostic problems. In young children or patients with an aberrant presentation of colitis, UC should always be considered in the differential diagnosis even if the pathology is not typical.

A diagnosis of established UC is based upon the combination of: basal plasmacytosis (plasma cells around (deep part of the lamina propria) or below the crypts (subcryptal)), heavy, diffuse transmucosal lamina propria cell increase and widespread mucosal or crypt architectural distortion (Figure-4A). Widespread mucosal or crypt architectural distortion, mucosal atrophy and a villous or irregular mucosal surface appear later (4 weeks or more). Decreasing gradient of inflammation from distal to proximal favours the diagnosis of UC in an untreated patient in addition to widespread crypt epithelial neutrophils (cryptitis and crypt abscesses) (Figure-4B). However these lesions may occur in other types of colitis. Lamina propria and intraepithelial neutrophils are absent in inactive or quiescent disease. Paneth cell metaplasia distal to the splenic flexure is a non specific feature. It is suggestive of a diagnosis of

UC in established disease. Severe, widespread mucin

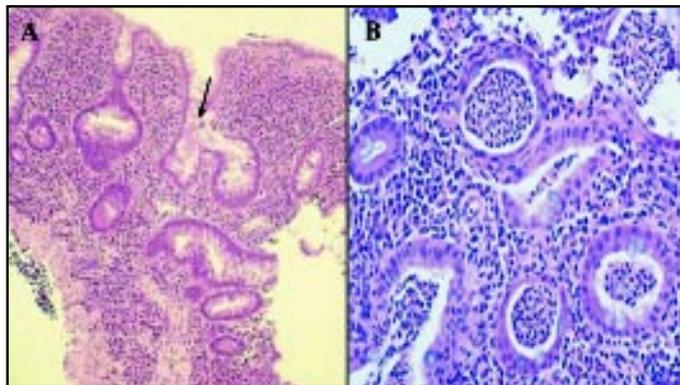


Figure-4 shows distortion of colonic architecture, with a loss of crypts and abnormal branching of the crypts (arrow) (A). Disordered architecture is useful in differentiating acute from chronic colitis. Histopathology in severe acute and chronic inflammatory process, with multiple crypt abscesses (arrow) (B).

depletion is helpful for the diagnosis of UC in active disease.

DEFINITIONS :

Remission

Remission is defined as complete resolution of symptoms and endoscopic mucosal healing (in clinical practice, a stool frequency ≤ 3 /day with no bleeding and no urgency). Remission defined by individual patients has 86% sensitivity and 76% specificity for a regulatory-defined remission (absence of visible blood and absent mucosal friability), indicating that sigmoidoscopy to confirm mucosal healing is generally unnecessary in practice.

Relapse

Combination of rectal bleeding with an increase in stool frequency and abnormal mucosa at sigmoidoscopy in a patient in remission was necessary to define relapse.

Steroid-refractory colitis

Active disease despite taking prednisolone up to 0.75 mg/kg/day for 4 weeks.

Steroid-dependent colitis

Patients who are i) either unable to reduce steroids below the equivalent of prednisolone 10 mg/day within 3 months of starting steroids, without recurrent active disease, or ii) who have a relapse within 3 months of stopping steroids. Although an alternative definition of relapse has been proposed as recurrence of symptoms within 30 days of completing a course of steroids, or steroids at a dose

of 15–25 mg/day for at least 6 months.

Medical management of active UC

Treatment strategy for active UC depends on the activity, distribution and pattern of disease. The disease pattern includes relapse frequency, course of disease, response to previous medications, side-effect profile of medication and extra-intestinal manifestations. The age at onset and disease duration may also be important factors.

Disease activity

It is most important to distinguish *severe UC* necessitating hospitalisation from those with mild or moderately active disease who can generally be managed as outpatients. The best validated and most widely used index for this remains that of *Truelove and Witts*: bloody stool frequency ≥ 6 /day and tachycardia (>90 bpm), or temperature >37.8 °C, or anaemia (haemoglobin <10.5 g/dL), or an elevated ESR (>30 mm/h) has severe UC (**Figure 3B**). Only one additional criterion in addition to the bloody stool frequency ≥ 6 /day is needed to define a severe attack. Active colitis should be confirmed by sigmoidoscopy before starting treatment, which also excludes other differential diagnosis (CMV colitis, rectal mucosal prolapse, Crohn’s disease, malignancy, or even irritable bowel syndrome and haemorrhoidal bleeding). *Clostridium difficile* toxin assay should also be done.

Treatment according to extent of disease Proctitis

A mesalazine (5ASA) 1 g suppository once daily is the preferred initial treatment for mild or moderately active proctitis. Mesalazine foam enemas are an alternative. Suppositories may deliver drug more effectively and are better tolerated than enemas. Combining topical with oral mesalazine or topical steroid is more effective than either alone and should be considered for escalation of treatment. Oral mesalazine alone is less effective. Refractory proctitis may require treatment with immunosuppressants and/or biologics.

Left sided colitis

Left-sided active UC of mild–moderate

severity should initially be treated with an aminosalicilate enema 1 g/day combined with oral mesalazine >2 g/day. Topical with steroids or aminosalicylates alone as well as mono-therapy with oral aminosalicylates is less effective than oral plus topical 5ASA therapy. Topical mesalazine is more effective than topical steroid. Once daily dosing with 5ASA is as effective as divided doses. Systemic corticosteroids are appropriate if symptoms of active colitis do not respond to mesalazine.

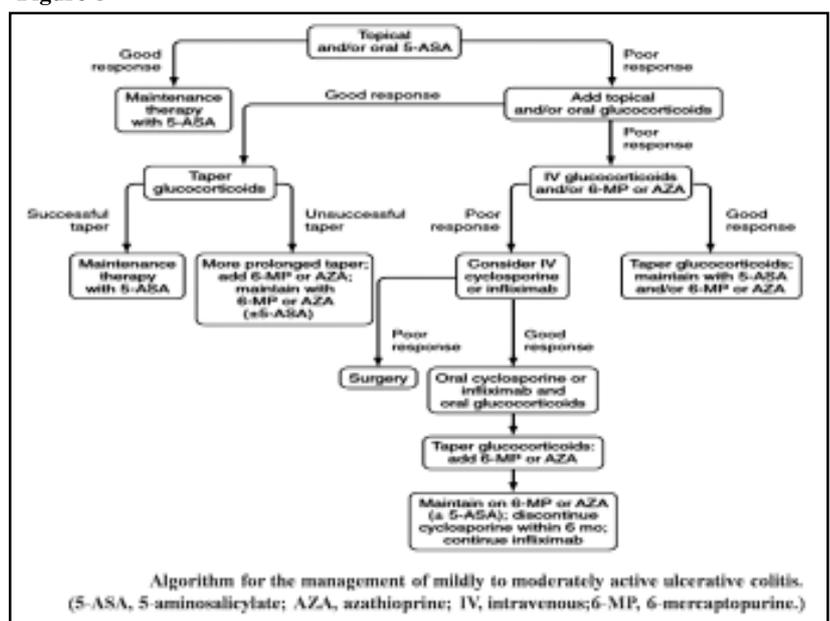
Severe left-sided colitis is usually an indication for hospital admission for intensive treatment with systemic therapy. Although most therapeutic trials of mild to moderate active colitis include patients with any disease distribution other than proctitis, there is clear evidence that both oral and topical mesalazine are effective for left-sided colitis compared to placebo.

Extensive ulcerative colitis

Extensive ulcerative colitis of mild–moderate severity should initially be treated with oral 5-ASA >2 g/day, which should be combined with topical mesalazine to increase remission rates if tolerated. Once daily dosing with 5ASA is as effective as divided doses. Systemic corticosteroids are appropriate if symptoms of active colitis do not respond to mesalazine. Severe extensive colitis is an indication for hospital admission for intensive treatment.

An algorithm for management of mild to moderate UC is given below (Figure-5).

Figure-5



Severe UC of any extent

Patients with bloody diarrhoea ≥ 6 /day and any signs of systemic toxicity (tachycardia >90 bpm, fever >37.8 °C, Hb <10.5 g/dL, or an ESR >30 mm/h) have severe colitis and should be admitted to hospital for intensive treatment. Enteric infections should be ruled out. Intravenous corticosteroids remain the mainstay of therapy. It is essential to ensure that the therapeutic alternatives for rescue of steroid-refractory disease (cyclosporine, tacrolimus, or infliximab) are considered early (on or around day 3 of steroid therapy) and that the decision making process is not delayed. Patients remaining on ineffective medical therapy including corticosteroids suffer a high morbidity associated with delayed surgery.

Conventional therapy.

Corticosteroids are generally given intravenously using methylprednisolone 60 mg/24 h or hydrocortisone 100 mg four times daily. Bolus injection is as effective as continuous infusion. Treatment beyond 7 to 10 days carries no additional benefit. Monotherapy with ciclosporin (normally at 2 mg/kg/day) is an useful option in severe colitis where steroids are best avoided, such as those with steroid-psychosis, osteoporosis or poorly controlled diabetes.

Other measures that are considered appropriate in addition to intravenous steroids include:

- Intravenous fluid and electrolyte replacement to correct and prevent dehydration or electrolyte imbalance. Potassium supplementation of at least 60 mmol/day is necessary. Hypokalaemia or hypomagnesaemia can promote toxic dilatation.
- Unprepared limited flexible sigmoidoscopy and biopsy to confirm the diagnosis and exclude Cytomegalovirus infection which is often associated with a steroid refractory disease course and requires appropriate treatment.
- Stool cultures and assay for *Clostridium difficile* toxin, which is more prevalent in patients with severe colitis and is associated with increased morbidity, mortality and health care costs. If detected appropriate, antibiotic therapy should be administered. Consideration should be given to stopping immunosuppressive therapy where possible, although this may not always be appropriate.
- Subcutaneous prophylactic low molecular weight heparin

to reduce the risk of thromboembolism which is increased in patients with IBD compared to controls, especially during a disease flare.

- Nutritional support if the patient is malnourished. Enteral nutrition is associated with significantly fewer complications than parenteral nutrition in acute colitis (9% vs 5%). Bowel rest through intravenous nutrition does not alter the outcome.
- Withdrawal of anticholinergic, antidiarrhoeal, NSAID and opioid drugs, which may risk precipitating colonic dilatation.
- Topical therapy (corticosteroids or mesalazine) if tolerated and retained, although there have been no systematic studies in acute severe colitis.
- Antibiotics only if infection is considered (such as in an acute, first attack of short duration, after recent admission to hospital or after travel to an area where amoebiasis is endemic), or immediately prior to surgery. Controlled trials of oral or intravenous metronidazole, tobramycin, ciprofloxacin or vancomycin in acute colitis have shown no consistent benefit in addition to conventional therapy.
- Blood transfusion to maintain haemoglobin above 8–10 g/dL.
- A multidisciplinary approach between the gastroenterologists and colorectal surgeons looking after the patient is essential.

Intravenous-steroid refractory UC of any extent

The response to intravenous steroids is best assessed objectively around the third day. Treatment options including colectomy should be discussed with patients with severely active UC not responding to intravenous steroids. Second line therapy with either ciclosporin or infliximab or tacrolimus may be appropriate. If there is no improvement within 4–7 days of salvage therapy, colectomy is recommended. Third line medical therapy may be considered at a specialist centre.

The timing of colectomy for severe colitis remains one of the most difficult decisions. Factors that predict the need for colectomy in acute severe colitis are clinical, biochemical and radiological markers.

Clinical markers

A stool frequency >12 /day on day 2 of iv corticosteroids was associated with rate of colectomy of

55%, whilst a frequency >8/day or a stool frequency between three and eight together with a CRP >45 mg/L on day 3 predicted colectomy in 85% on that admission: the *Oxford Criteria*. Similarly a stool frequency $\times 0.14$ CRP being e^{-8} on day 3 predicted colectomy in 75%: the *Sweden Index*.

Biochemical markers include a high CRP, low albumin and pH. In one study an ESR >75 or a pyrexia >38 °C on admission was associated with a 5–9-fold increase in the need for colectomy. Lack of response to steroids was predicted by <40% reduction in stool frequency within 5 days.

Radiological/endoscopic criteria include the colonic dilatation >5.5 cm or mucosal islands on a plain abdominal radiograph (75% need colectomy). A retrospective study showed that the presence of an ileus (3 or more small bowel loops of gas) had 73% chance of colectomy. Depth of colonic ulcers predicted need for colectomy. A numerical score combining mean stool frequency over three days, presence or absence of colonic dilatation and hypoalbuminaemia (<30 g/L) on admission was associated with the need for colectomy in up to 85%.

Cyclosporin.

Cyclosporin is a calcineurin channel inhibitor and when used as 2 mg/kg/day will avoid colectomy in short term in 76-85%. The median time to response is 4 days which allows timely colectomy in non-responders. However, the narrow therapeutic index of cyclosporin and its side-effect profile (including mortality rates of 3–4%) have limited acceptability. It should be avoided in those with low cholesterol or magnesium due to increased risk of neurological side-effects. Successful transition to an oral thiopurine and being thiopurine-naive at baseline has been confirmed as factors that reduce the risk of long term colectomy. Patients with UC refractory to adequate thiopurine therapy are less suitable candidates for cyclosporin rescue therapy.

Tacrolimus

Tacrolimus is a calcineurin inhibitor with similar mechanism of action like cyclosporin. Case series have shown broadly similar results to cyclosporine after both intravenous (0.01 to 0.02 mg/kg) and oral (0.1 to 0.2 mg/

kg) administration. The long term cumulative colectomy free survival in has been reported to be 57% at 44 months, although this included a very heterogeneous population.

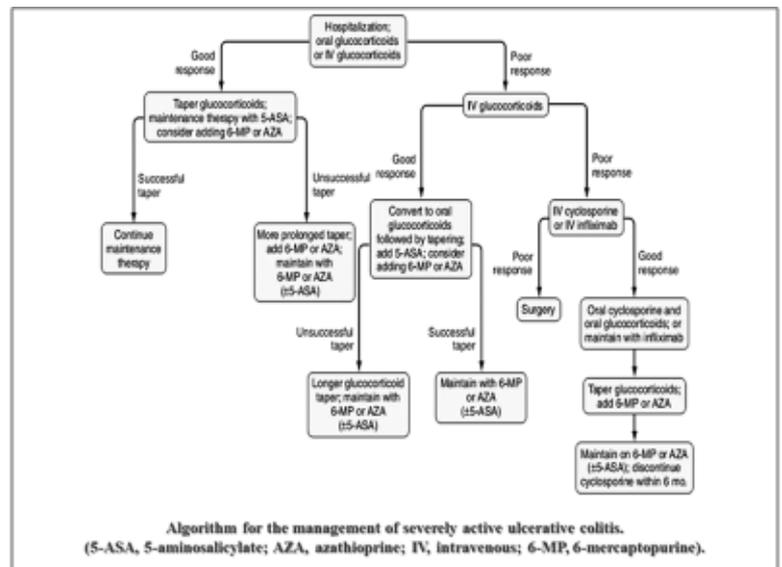
Infliximab

Infliximab as a single dose (5 mg/kg) is an effective salvage therapy in severe UC refractory to iv steroids. Case series reports 20-75% colectomy rates after infliximab for iv steroid-refractory UC. Patients with 2 or more infusions, high baseline disease activity, seronegative for ANCA or homozygous for IL23R gene have increased short term response.

Third line medical therapy

In general only a single attempt at rescue therapy with a calcineurin inhibitor or infliximab should be considered before referral for colectomy. However, treatment success has been reported for sequential use of calcineurin inhibitors and infliximab after iv corticosteroids. In highly selected cases, after careful discussion between the patient, gastroenterologist and colorectal surgeon, third line medical therapy can be considered in a specialist referral centre.

An algorithm for managing severe UC is given below (Figure-6).



Complications of severe UC

Toxic megacolon.

It is defined as total or segmental non-obstructive colonic dilatation $e^{-5.5}$ cm associated with systemic toxicity. Approximately 5% episodes of acute severe colitis

will have toxic dilatation. Risk factors include hypokalaemia, hypomagnesaemia, bowel preparation, and anti-diarrhoeal therapy. Earlier diagnosis of severe colitis, more intensive care and earlier surgery have reduced the incidence and mortality of toxic megacolon. In addition to iv hydrocortisone, empirical oral vancomycin should be considered until stool is confirmed negative for *Clostridium difficile* toxin. An opinion from an experienced colorectal surgeon is required on the day of admission. There is a limited window of opportunity for medical treatment to work and that if there is no improvement early colectomy will be necessary.

Perforation

It is the most serious complication of acute severe colitis and is often associated with inappropriate total colonoscopy or toxic dilatation where colectomy has been inappropriately delayed. It carries a mortality of up to 50%. Other complications include massive haemorrhage, and thromboembolism including cerebral sinus thrombosis.

Early relapse

Patients who have an early (<3 months) relapse require further induction therapy, but should also commence azathioprine or mercaptopurine to reduce the risk of a subsequent relapse. Opinion is divided whether to use the same induction treatment as before to achieve remission or to use more potent therapy. It is generally unnecessary to re-evaluate the distribution of disease unless this will influence medical or surgical management. Continued medical therapy that does not achieve steroid-free remission is not recommended.

‘Steroid-dependent’, active ulcerative colitis

Patients with steroid-dependent disease should be treated with azathioprine/mercaptopurine. Azathioprine is significantly more effective than mesalazine at achieving clinical and endoscopic remission in the treatment of steroid-dependent UC. Thiopurines should be the first choice of therapy for patients who flare when steroids are withdrawn. Patients with active disease despite steroid therapy require appropriate induction therapy, including consideration of anti-TNF therapy (adalimumab or infliximab).

Oral steroid-refractory ulcerative colitis

Outpatients with moderately active steroid refractory disease should be treated with anti TNF therapy or tacrolimus, although surgical options or admission for parenteral steroid therapy could also be considered. For active UC that is refractory to steroids, other causes of persistent symptoms including coexistent cytomegalovirus, *Clostridium difficile* or cancer should be considered. If active steroid-refractory UC is confirmed, alternative therapy to induce steroid-free remission is required. Anti-TNF therapy has clear evidence of benefit in this patient group.

Immunomodulator-refractory ulcerative colitis

Patients with moderately active UC refractory to thiopurines should be treated with anti TNF therapy or tacrolimus although colectomy should also be considered. These patients are best reassessed by endoscopy and biopsy to confirm the diagnosis and exclude complications. In the absence of contraindications, anti TNF therapy should be considered. Discussion with the patients is required as to the relative risks and benefits of immunosuppressive therapy compared to colectomy, which may be a more appropriate option for some patients.

Therapy-specific considerations & side effects

Aminosalicylates.

Delivery systems can be divided into azo-compounds, controlled release, pH-dependent (either pH6 or pH7) and composite (pH-dependent combined with controlled release). Available data do not suggest a difference in efficacy between any of the 5-ASA preparations for active UC. Doses of ≥ 2.0 g/day are more effective for remission. Once daily dosing is as effective as divided doses. Mesalazine has been shown to be as effective as sulfasalazine for inducing response or remission in and is better tolerated.

Mesalazine intolerance occurs in up to 15 %). Diarrhoea (3%), headache (2%), nausea (2%), rash (1%) and thrombocytopenia (<1%) are reported, but overall all new 5-ASA agents are safe. Acute intolerance (3%) may resemble a flare of colitis. Idiosyncratic Renal impairment (including interstitial nephritis and nephritic syndrome) is rare. Patients with pre-existing renal

impairment, significant co-morbidity or those taking nephrotoxic drugs should have renal function monitored during therapy (creatinine and full blood count should be monitored every 3–6 months). Side effects of oral 5-aminosalicylates are shown below.

Side Effects of Sulfasalazine & Oral 5-Aminosalicylates

Dose-Related

Alopecia
Anorexia
Back pain
Folate malabsorption (with sulfasalazine)
Headache
Nausea, vomiting, dyspepsia

Non-Dose-Related

Agranulocytosis, aplastic anemia
Arthralgia
Colitis
Fever
Fibrosing alveolitis, pulmonary eosinophilia
Hemolytic anemia (Heinz bodies)
Hepatitis
Hypersensitivity skin rashes (occasionally with photosensitivity)
Male infertility (with sulfasalazine)
Pancreatitis
Pericarditis, myocarditis

Corticosteroids

There is definite clinical benefit of standard glucocorticoids over placebo for UC remission. Adverse effects are depicted in figure shown below.

Side Effects of Glucocorticoids

Cutaneous

Acne
Impaired wound healing
Purpura, Ecchymoses, petechiae
Striae

Endocrine

Adrenal insufficiency
Cushingoid appearance

Gastrointestinal

Dyspepsia
Dysphagia/odynophagia (candidiasis)

Infectious complications

Numerous pathogens

Metabolic

Electrolyte imbalance, hypokalemia
Fluid retention
Growth retardation
Hyperglycemia, secondary diabetes mellitus
Hyperlipidemia, altered fat distribution
Hypertension

Musculoskeletal

Myopathy
Osteonecrosis
Osteoporosis

Neuropsychiatric

Anxiety, mood swings
Depression

Insomnia

Psychosis

Ocular

Cataracts
Glaucoma

Anti-TNF therapy

Infliximab was effective for inducing clinical remission, promoting mucosal healing, and reducing the need for

colectomy in the short term. Three infusions at 0, 2, and 6 weeks was more effective than placebo in inducing clinical remission at week 8. A single infusion of infliximab was also more effective than placebo in reducing the need for colectomy within 90 days after infusion. Adalimumab & golimumab are also effective.

Anti-TNF therapy is relatively safe if used for appropriate indications. Nevertheless, there is a risk of serious infection, demyelinating disease and associated mortality.

Other biological therapies

Vedolizumab (MLN-02-47 integrin antagonist), vedolizumab (anti-CD3 monoclonal antibody), basiliximab & daclizumab (CD25 inhibitor), abatacept (CTLA4-Ig: a costimulatory receptor inhibitor), interferon-alpha, tofacitinib (Anti-JAK 1, 2, and 3) are being used in clinical trials.

Thiopurines

Immunomodulators should be started in steroid-dependent and steroid-refractory patients. Their successful introduction is associated with colectomy-free survival in patients with severe UC treated with ciclosporin & infliximab to induce remission. Side effects are shown in figure below.

Side Effects of Azathioprine and 6-Mercaptopurine

Abnormal liver biochemical test results
Bone marrow suppression
Hypersensitivity reactions (fever, rash, arthralgia)
Infections
Lymphoma
Nausea, abdominal pain, diarrhea
Pancreatitis

Cyclosporin & Tacrolimus

Side effects are shown in figure below

Side Effects of Cyclosporine

Anaphylaxis	Infections
Diarrhea	Nausea, vomiting
Electrolyte abnormalities	Opportunistic infections
Gingival hyperplasia	Paresthesia
Headache	Renal insufficiency
Hepatotoxicity	Seizure
Hirsutism	Tremor
Hypertension	

Other treatment modality that has been used in UC are Methotrexate, leucocytapheresis, antibiotics

Surgery

Surgery for UC has been refined to offer patients needing colectomy a better quality of life. Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the gold standard with preserved anal route of defaecation. Nevertheless, bowel function is not restored to normal and both functional outcome and quality of life after IPAA have still to be compared to living with an ileostomy. IPAA is probably one of the most frequently described procedures in colorectal surgery. The indications and timing of surgery for UC are given below.

Indications for Surgery in UC

Colonic dysplasia or carcinoma
Colonic hemorrhage, uncontrollable
Colonic perforation
Growth retardation
Intolerable or unacceptable side effects of medical therapy
Medically refractory disease
Systemic complications that are recurrent or unmanageable
Toxic megacolon

Technical considerations

Surgery for acute severe colitis

A *staged procedure* (subtotal colectomy first) is recommended in acute cases when medical therapy fails, or if prednisolone 20 mg daily or more is used for more than 6 weeks. Joint surgical and gastroenterology care remains essential. Whilst medical therapy is effective in many, delay in appropriate surgery is detrimental. A subtotal colectomy with an ileostomy will cure the patient from colitis, normalise nutrition and give the patient time to consider the option of an IPAA or permanent ileostomy. It also allows the pathology to be clarified and Crohn's to be excluded. It is a relatively safe procedure even in the critically ill patient and if the appropriate expertise is available it is safe to perform laparoscopic surgery.

Managing the rectal remnant

When performing a colectomy in emergency circumstances, the whole rectum and the inferior mesenteric artery should be preserved. This facilitates subsequent pouch surgery. Whether to preserve additional recto-sigmoid colon and how to deal with bowel closure is left to the surgeon's decision. Leaving as little rectum as possible (i.e. dividing the middle rectum within the pelvis) is not to be recommended, because it renders subsequent proctectomy difficult, with a probable increase in the risk

of pelvic nerve injury. The alternatives are to divide the rectum at the level of the promontory (i.e. at the proper rectosigmoid junction), or to leave in addition the distal part of the sigmoid colon. When performing pouch surgery, the maximum length of anorectal mucosa between the dentate line and the anastomosis should not exceed 2 cm. A common complication of using a stapling technique to perform the ileo-anal anastomosis is leaving a remnant of anorectal mucosa above the dentate line. This can be a cause of persistent inflammation ('cuffitis'), with pouch dysfunction and a risk of dysplasia or (very rarely) cancer. Careful surgical technique even in the face of a narrow male pelvis should prevent this from happening. Done well, the stapled anastomosis seems to have better outcomes, particularly with regard to soiling, faecal leakage and social restriction.

Role of covering ileostomy for restorative proctocolectomy

When performing a restorative proctocolectomy a covering loop ileostomy is generally recommended, but can be avoided in selected cases. One of the main complications of IPAA surgery which compromises the outcome, is an anastomotic leak in pouch. There is emerging evidence that defunctioning the distal anastomosis may reduce this risk. Presence of thick abdominal wall and a short small bowel mesentery does not justify stoma.

Follow-up

General pouch follow up

Follow up should include looking for signs of pouchitis which develops in approximately 20–30%, which may be recurrent or persisting. Patients with high risk features, such as: PSC or previous malignancy or dysplasia should undergo long term surveillance for pouch or pouch-anal dysplasia, which invariably occurs in patients operated with dysplasia or cancer already present in the specimen at primary surgery.

Female fecundity or fertility is reduced after IPAA (30-70%), probably due to adhesions affecting the fallopian tubes. There is no reduction in fecundity associated with an *ileorectal anastomosis* (IRA) as it does not induce pelvic adhesions to nearly the same extent as an IPAA. IRA also does not disturb sphincter function, unlike IPA.

Surgical choices in addition to restorative proctocolectomy.

There is no defined age limit for performing an IPAA. Despite the evidence of higher levels of co-morbidity in patients over the age of 65, IPAA appears safe and effective. However, an increased frequency of pouchitis or anastomotic stricture has been reported. Deterioration in pouch function with advancing age applies to all patients undergoing IPAA and faecal incontinence in particular, with evidence that this may be more pronounced in the elderly. However, it appears that despite this burden of worsening continence patients over the age of 65 with IPAA still retain a good quality of life. Decisions about what operation to perform on this elderly group must therefore be tailored to the individual.

Continent ileostomy

This is still a viable option when there is no possibility of performing an ileal pouch anal anastomosis, or when the IPAA fails for other reasons than pouchitis, or when the patient specifically requests this solution. The continent ileostomy ('Kock pouch') was the forerunner to the IPAA. It is a complex procedure with a high risk of re-operation. However, well motivated patients with a functioning continent ileostomy patients report excellent quality of life with a next-to-normal body image. Furthermore a failed pelvic pouch can still be converted to a continent ileostomy which may restore a good quality of life.

Ileorectal (IRA) anastomosis

An IRA should be considered only in special cases (such as for reasons of fertility). Long term surveillance of the retained rectum is advised. An IRA is not only non-curative, but also leaves likelihood of persistent symptoms from refractory rectal inflammation and a risk of later cancer. Even so, recent series show a better than expected durability, with half of the patients still living with an IRA after 10 years. Its role in the management of women facing surgery before they have completed their family is

discussed above. Despite the reduced risk of subsequent colitis-related dysplasia and malignancy following colectomy, interval surveillance of the retained rectum is still recommended.

Cancer surveillance of the rectal remnant after colectomy

For patients with colectomy and ileostomy, surveillance of the retained rectum is appropriate. Proctectomy is a major operation with a potential for delayed wound healing and risk of sexual dysfunction both in women and men. Alternatively, a retained rectum can lead to a significant reduction in quality of life. The issue of cancer risk although low, in the retained mucosa is also unresolved. Recommendation is that retained rectal stumps should undergo periodic surveillance along the lines of patients with UC.

Laparoscopic pouch surgery

Laparoscopic restorative proctocolectomy with an IPAA is both feasible and safe with faster recovery, better cosmesis, reduced burden of adhesions and thus improved fecundity.

In summary, UC is a lifelong disease with course having remissions and intermittent relapses with occasional complications that can be life threatening. Patient education & close coordination is of utmost importance between patient and treating gastroenterologist for a better management.

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Unusual Presentation of Takayasu Arteritis with Dilated Cardiomyopathy, Aortic Aneurysm and Chronic Kidney Disease in a young female : a Case Report

B Barman*, M Lyngdoh*, T Beyong**, S B Warjri**

Abstract

Takayasu arteritis is a rare inflammatory vasculitis with various clinical manifestations. It predominantly affects young female. Dilated cardiomyopathy together with aortic aneurysm and chronic renal failure as a presenting feature in same patient with Takayasu arteritis is very rare. It is important to keep high degree of suspicion, especially in young female presented with cardiomyopathy, otherwise diagnosis can be missed.

INTRODUCTION :

Takayasu arteritis (TA), also known as pulseless disease, non specific aorto arteritis or occlusive thromboaropathy is a relatively rare inflammatory vasculitis that chiefly affects the aorta and its major branches most frequently in young female with median age of onset 25 years. Geographically although it has been described worldwide, the disease is most commonly seen in Southeast Asia mainly in Japan and India and also in Mexico. Lesions may be stenotic, occlusive or aneurysmal. Although cardiac involvement occurs eventually in nearly one third of patients, but cardiomyopathy is a very rare manifestation. Here we are reporting a case of TA presenting with rare manifestation of dilated cardiomyopathy, aortic aneurysm and chronic kidney disease in the same patient.

CASE REPORT :

A 32 years old female presented with history of sudden onset breathlessness for two days. There was no associated history of diabetes mellitus, hypertension or any cardiac disease in the past. On physical examination she was thin built, pale, tachypnoeic with a respiratory



Fig 1: A large aneurysmal sac is seen arising from the descending thoracic aorta, projecting anterior medially.

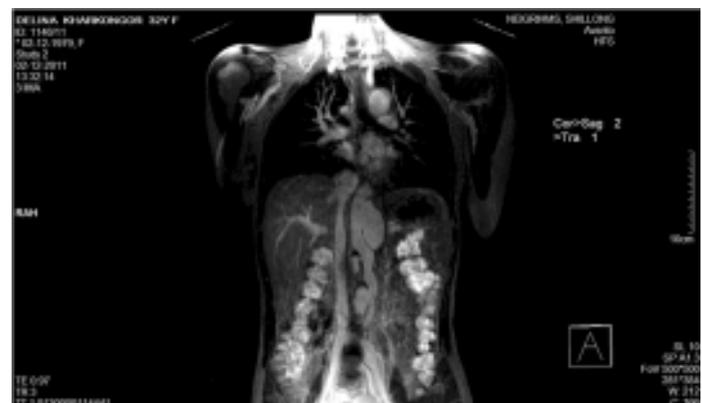


Fig 2: Multiple sacular aneurysms are seen arising from abdominal aorta. A sacular aneurysm is seen arising from abdominal aorta, located just below the diaphragm involving the celiac artery origin

rate of 30 per minute. Her radial and brachial pulse rate was 102/minute, regularly regular in both the upper limbs.

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Fig 3: A large aneurysm is arising from aorta at the level of renal arteries, incorporating the right renal artery ostium.

Lower limb pulses were equal in both sides but more feeble than both the upper limb pulses. Blood pressure in the upper limbs was 180/100 mm Hg whereas it was 140/90 mm Hg in the lower limbs with a pulse pressure difference of 40mmHg. She had signs of heart failure like raised jugular venous pressure, bilateral pitting pedal edema and tender hepatomegaly, bibasilar fine crepitations in the infrascapular areas and LV S3 gallop. Systolic murmur was heard in the mitral area. Hemoglobin was 7.8 gm/dl. ESR: 59 mm AEFH, urine protein was 1+, C Reactive Protein was positive, blood urea and serum creatinine were 99 mg/dl and 3.3 mg/dl respectively. Echocardiography report showed dilated cardiomyopathy with moderate left ventricular systolic dysfunction (ejection fraction 40%) with mild mitral regurgitation with descending thoracic aneurysm with aortic aneurismal sac with spontaneous echo contrast. Sonography of abdomen showed decreased size of both kidneys (left kidney: 9.27cm, right kidney: 8.17cms in diameters) with loss of corticomedullary junction with hepatomegaly. MR angiography showed multiple saccular aneurysms arising from abdominal aorta with one of the aneurysm located just below the diaphragm involving celiac artery origin. A large aneurismal sac is seen arising from the descending thoracic aorta projecting anteromedially. She was treated with medical management for heart failure and nephropathy.

DISCUSSION :

Takayasu arteritis is a chronic progressive inflammatory disease of large and medium sized arteries seen mostly in Asian and Hispanic origin with female preponderance in their 2nd and 3rd decade with wide

geographic variation with ratio of 8:1 in Japan, 4:1 in India and 1.2:1 in Israel¹. Although it was first described by Dr R Adams in 1827, the disease was named after the Japanese ophthalmologist Mikito Takayasu who first reported it in 1908. The disease is classified into different types according to the site of involvement of the aorta and its branches as follows: localized involvement of arch of aorta and its branches (type I), in whole of thoraco-abdominal aorta and its branches without involvement of the arch (type II), combined features of both I and II (type III), pulmonary involvement in addition to arch (type IV), coronary involvement (type V)².

Majority of patients of TA present with non-specific symptoms like fatigue, malaise, fever, weight loss, arthralgia, skin rash. The vascular manifestations of TA are either due to vascular insufficiency (from stenosis, occlusion, aneurysm), systemic inflammation or both. Most common vascular presentations are claudication (35%), reduced or absent pulse (25%), carotid bruit (20%), hypertension (20%), carotidynia (20%), lightheadness (20%) and asymmetry arm blood pressure (15%). Presentation is quite different in India where asymmetry of pulse is very much common (96%) followed by hypertension (72%), renal failure (30%), claudication 25%), CNS symptoms (22.5%), eye changes (8.1%) and skin manifestations (3.8%)³.

American College of Rheumatology (1990) has selected six criteria for diagnosis of TA. This includes onset before age 40 year, limb claudication, decreased brachial arterial pulse, unequal arm blood pressure > 10 mmHg, subclavian or aortic bruit, angiographic evidence of narrowing, occlusion or aneurysm of aorta and its major branches, or large limb arteries. The presence of three or more of six criteria is sensitive (91%) and specific (98%) for the diagnosis of TA⁴.

As the clinical presentation of TA varied widely in distribution, it is very difficult to assess true incidence of cardiac involvement. Different literature from India has shown Hypertension as one of the most frequent clinical presentation followed by aortic regurgitation probably resulting from aortic root dilation. The association of TA and cardiomyopathy is not very common phenomenon. It was first described in an autopsy case series of 10 patients of aortoarteritis where 4 cases had congestive cardiomyopathy. The etiology of cardiomyopathy in TA is

not known, probably there is an autoimmune reaction may be due to infectious agents or disease process itself that may lead to cardiomyopathy⁵.

Isolated aneurysm in TA is very rare (2-26.7%). The aneurismal symptoms include a pulsatile mass, embolism from mural thrombus and ruptured leading to hemothorax or death⁶. The rate of growth and risk of rupture of Takayasu aneurysm are thought to be lower than those to atherosclerotic aneurysm that may be due to more calcium deposition and more severe scar formation

There are very few reported studies showing presentation of dilated cardiomyopathy, aortic aneurysms and chronic kidney disease together in a patient with Takayasu arteritis. Our case was a young female with dilated cardiomyopathy, aortic aneurysm and chronic kidney disease in congestive heart failure with diminished lower limb arterial pulsations.

CONCLUSION :

Although rare, Takayasu arteritis can present with aortic aneurysm, chronic kidney disease and dilated cardiomyopathy in the same patient. A strong clinical suspicion together with detailed physical examination can help to early diagnosis and reduce other complication of vaculities which may be devastating.

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Successful primary PCI in an elderly with significant thrombus burden

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Abstract

It is well established that timely primary percutaneous coronary intervention (PCI) in patients with ST elevation myocardial infarction (STEMI) improves survival compared to medical therapy alone. We report a 70 year old gentleman with an acute inferior wall STEMI of two hours duration who underwent successful primary PCI. The significant thrombus burden in this particular patient and the combined use of intracoronary tirofiban and manual thrombus aspiration using the Export Catheter (Medtronic) leading to excellent clinical and angiographic results makes this case unique and worth presenting. The technical aspects of primary PCI in thrombus containing lesions, role of combined manual thrombus extraction using the low profile export catheter and the intracoronary use of GPIIb IIIa inhibitor, Tirofiban is discussed.

Key Words : Acute ST elevation myocardial infarction, Primary PCI, Intracoronary thrombus, Export catheter, GPIIb IIIa inhibitor Tirofiban

INTRODUCTION :

When PCI is used in lieu of thrombolytic therapy, it is referred to as primary PCI. It involves opening up or reperfusing the infarct related artery using a percutaneous catheter based strategy (using balloon catheter over a guidewire, low profile aspiration catheters and coronary stents). Primary PCI is the approach of choice for acute ST elevation myocardial infarction but is not available in most hospitals especially in this part of the country. Primary PCI for STEMI is indicated in patients who present within 12 hours from the onset of symptoms and in whom the infarct related artery can be recanalized within 90 minutes of presentation. The advantages of primary PCI include early and complete reperfusion and reduced bleeding complications relative to thrombolytic therapy.

CASE PRESENTATION :

This 70 year old diabetic and hypertensive gentleman

from Guwahati was attended to after receiving an emergency call at 12.30 AM when he complained of severe retrosternal chest pain associated with profuse sweating of 2 hours duration. A quick clinical examination in the emergency department revealed a BP of 90/60 mmHg, pulse rate of 100/min, chest bilaterally clear and no left ventricular S3, murmur or rub on cardiovascular examination. His ECG showed ST segment elevation in leads II, III and aVF and ST depression and T wave inversion in leads I and aVL (Figure I). Two dimensional



Figure I : Initial ECG on presentation showing ST segment elevation in leads II, III and aVF and ST depression in leads I and aVL suggestive of Acute Inferior wall ST elevation myocardial infarction.

transthoracic echocardiogram revealed hypokinesia of right coronary artery territory with a left ventricular ejection fraction of 50%. His cardiac biomarkers were positive (CK-MB and Troponin-I).

With a diagnosis of acute inferior wall myocardial infarction of 2 hours duration, he was taken to the cardiac cath lab within 20 minutes of arrival with the intention of performing Primary PCI. The patient was pretreated with

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325 mg of Aspirin and 600 mg loading dose of Clopidogrel was administered on arrival. Vascular access was established via right femoral artery and pre-procedure temporary pacemaker was implanted as he started having complete heart block with a rate of 40/min. Coronary angiogram revealed normal left main, Left anterior descending (LAD) coronary artery had ostial plaque and distal disease and Left circumflex (LcX) coronary artery showed multiple stenosis. Both LAD and LcX showed good antegrade flow (Figure II A). The right coronary artery (RCA) was totally occluded in the proximal segment just after origin and was the culprit infarct related artery (IRA) in this case (Figure II B).

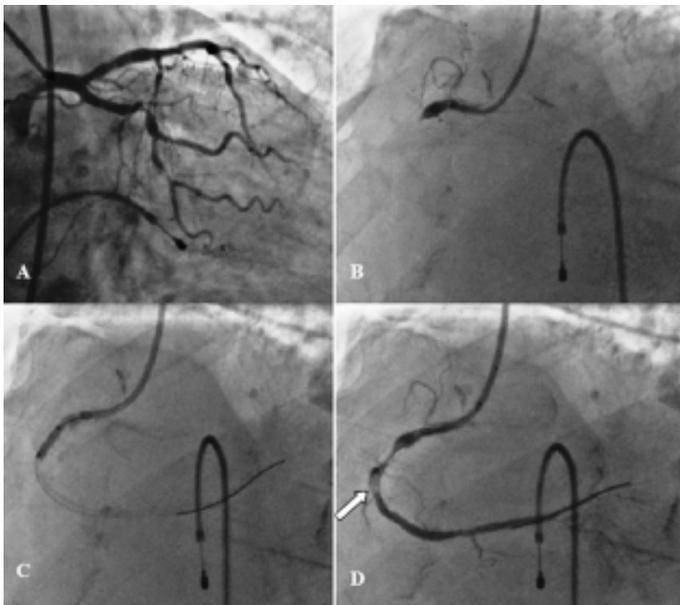


Figure II : A. Coronary angiogram revealed normal left main, LAD had ostial plaque and distal disease and LcX showed multiple stenosis. Both LAD and LcX showed good antegrade flow. B. RCA totally occluded in the proximal segment just after origin. C. Predilatation with 2.5 X 15 mm balloon. D. Antegrade flow established revealing a concentric tubular stenosis in the proximal RCA with a large thrombus (Arrow) just distal to the stenosed segment.

The RCA was hooked with JR 3.5 6F guiding catheter and the lesion was crossed with BMW guidewire. The lesion was predilated with 2.5 X 12 mm SPRINTER LEGEND balloon and antegrade flow was established (Figure II C). Cine angiogram revealed a concentric tubular stenosis in the proximal RCA with a large thrombus just distal to the stenosed segment (Figure II D, Arrow). Intracoronary tirofiban (20 mcg/Kg) was given followed by manual extraction of the thrombus using the EXPORT CATHETER which led to complete clearing of the thrombus (Figure III A, arrow showing

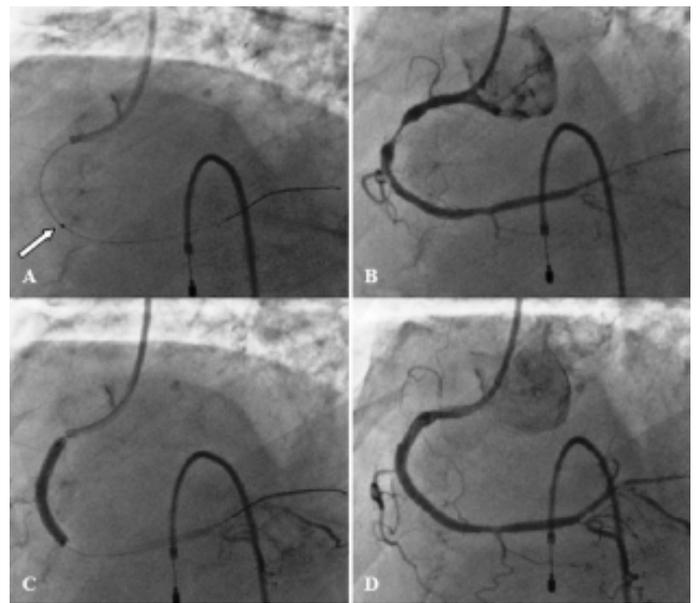


Figure III : A. Manual thrombus extraction using the Export catheter (Arrow). B. Complete clearing of the thrombus. C. A 3 X 30 mm RESOLUTE INTEGRITY drug eluting stent deployed across the lesion. D. TIMI III flow achieved in the infarct related artery.

tip of export catheter and B). A 3 X 30 mm RESOLUTE INTEGRITY drug eluting stent was deployed across the lesion at 15 atmosphere for 25 seconds (Figure III C) and TIMI III flow was achieved (Figure III D). On table, his angina was relieved, BP significantly improved (130/80mmHg) and intrinsic heart rate resumed (earlier just before the procedure he was dependent on the temporary pacemaker). The procedure was done under 5000 IU of unfractionated heparin and intracoronary Tirofiban. An activated clotting time (ACT) of 300 seconds was achieved at the end of the procedure. He received intravenous Tirofiban infusion for the next 16 hours (0.15 mcg/Kg/min). Post procedure ECG in the morning revealed complete resolution of ST segment elevation (Figure IV).

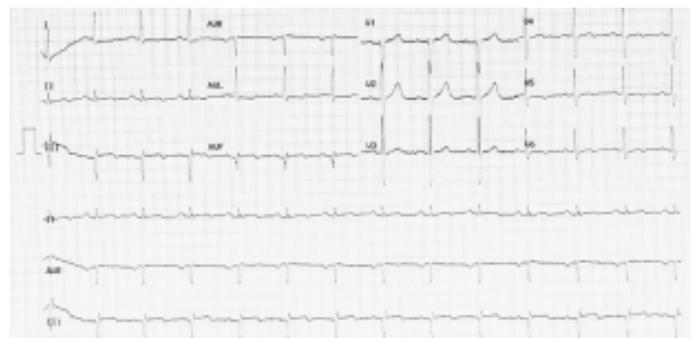


Figure IV : Post procedure ECG in the morning revealed complete resolution of ST segment elevation.

DISCUSSION :

Presence of a significant, angiographically apparent coronary thrombus during Primary PCI increases the risk for procedural complications. Thrombotic burden is often large in patients with prolonged symptom duration or if the IRA is a large diameter vessel such as an RCA or a saphenous vein graft. Large coronary thrombi may fragment and embolize during PCI or may extrude through gaps between stent struts placed in the vessel, thereby risking lumen compromise or thrombus propagation and acute thrombosis of the treated vessel. In addition, large coronary thrombi can embolize to other coronary branches or vessels or dislodge and compromise the cerebral or other vascular beds.

In the setting of STEMI, manual catheter aspiration of thrombus before stenting reduce the likelihood of distal embolization in the IRA branches or microcirculation resulting in “slow” or “no reflow” phenomenon. Manual catheter aspiration also reduce the risk for future ischemic events, including stent thrombosis and mortality. The Export aspiration catheter (Medtronic) is a rapid-exchange 6Fr compatible thrombus aspirating catheter. It has a soft, flexible non-traumatic tip, with an oblique aspiration tip design. There is a main lumen (the aspiration-infusion lumen) and a smaller lumen for the guidewire. Thrombus is aspirated by means of continuous negative pressure maintained by a syringe. Since the Export catheter is a low profile aspiration catheter, the risk for distal particulate embolization and device related trauma is low. A comprehensive meta analysis of randomized trials suggests that simple manual thrombus aspiration before PCI reduces mortality in patients undergoing primary PCI.

In this index case with significant thrombus burden, the combined use of intracoronary (i/c) GPIIb IIIa inhibitor, Tirofiban and manual thrombus aspiration led to excellent clinical and angiographic results. There is paucity of data on this approach in patients with STEMI. In a small study comparing the probable synergistic effect of the combination of i/c Tirofiban and manual thrombus aspiration versus intravenous Tirofiban alone during primary PCI in

patients with STEMI demonstrated superior clinical outcomes (superior ST segment resolution at 60 minutes, better myocardial blush grade and significantly less combined MACE at 30 days) than intravenous Tirofiban alone.

CONCLUSION :

Primary PCI is the treatment of choice in the management of acute STEMI. Thrombus containing lesions are frequently encountered at coronary angiography in such clinical scenario. Although not much supporting data is available at present, combined use of intracoronary GPIIb IIIa inhibitor, Tirofiban and manual thrombus extraction during primary PCI with significant thrombus burden is not only feasible but also results in superior clinical and angiographic outcomes.

Therefore, current management of patients with STEMI is not only a mechanical restoration of flow within the IRA, but also includes a system of early diagnosis and rapid transfer to PCI-capable centres, selection of optimal adjunctive pharmacotherapy and finally PCI procedures with dedicate devices. All these components are necessary for the eventual success of the treatment.

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Intrahepatic Cholestasis in Sickle Cell Disease : A Case report from Upper Assam

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Abstract

Intrahepatic cholestasis (SCIC) is an uncommon but potentially fatal complication of sickle cell disease, with a high death rate, observed mainly in patients with homozygous sickle cell anemia. Its presentation ranges from a benign conjugated hyperbilirubinemia to a fulminant hepatic failure. We reported a case of intrahepatic cholestasis in the sickle cell anemia in our hospital. Previous case reports showed that intrahepatic cholestasis in sickle cell anemia is a fatal condition requiring exchange transfusion, as the only treatment but here we describe that aggressive conservative management along with packed cell transfusion can revert this condition. The patient described here suggests that sickling within the liver, previously reported to be a serious and even fatal syndrome, usually is a benign and self limited process.⁸

KEYWORDS: *Intrahepatic cholestasis, Sickle cell anemia.*

INTRODUCTION:

Intrahepatic cholestasis is an uncommon but potentially fatal complication of sickle cell disease, with a high death rate observed mainly in patients with homozygous sickle cell anemia. Its presentation ranges from a benign conjugated hyperbilirubinemia to a fulminant hepatic failure.¹⁻⁴This syndrome is characterized by abdominal pain in the upper right quadrant, enlarged liver, light stools, marked conjugated hyperbilirubinemia and variable elevation of aminotransferases levels, but usually not more than 1-3 times normal. In more severe cases, renal dysfunction and alteration of coagulation tests can be observed. The diagnosis requires exclusion of viral hepatitis and cholecystitis/cholelithiasis. Treatment patterns are not well established and range from supportive care to exchange transfusion. However, early recognition of severe cases and aggressive exchange transfusion of red blood cells (RBCs) are considered crucial to attain a favourable outcome.^{5,6,7} Herein, we have reported a case

of Intrahepatic cholestasis with a favourable outcome after aggressive conservative management and packed cell transfusions.

CASE REPORT :

Patient aged 17 yrs, male hailing from Milanpur, Sonari, student by occupation presented with yellowish discoloration of eyes, skin and urine for 1 month without associated itching and clay coloured stool. There was no history of herbal medication, abdominal pain, blood transfusion, drug abuse or any sexual exposure. However, there was associated generalized weakness and decreased appetite with past history of jaundice on and off since 12 yrs of age. Fever started 10 days after appearance of yellowish discoloration which was high grade, intermittent in nature with chills and rigor without any history of burning micturition, abdominal pain and it subsided on taking medications.

On examination, pallor & icterus were present, temperature was recorded to be 102.6 æ% F. All the systems were within normal limit. Investigations revealed Hb% -5.22, TC-40,00, ESR-85, Serum bilirubin-18.22, Direct Bilirubin-13.5, Indirect Bilirubin-4.7, ALT-82, AST-123, ALP-600. All the viral markers were negative. Initially, ofloxacin was started along with Ursodeoxycholic acid and IV Fluids and O₂ inhalation.

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Ofloxacin was discontinued after 4 days and Meropenem was started since the total count was very high. Malaria, Typhoid, Leptospira and Dengue serology was negative, so Serum for Scrub Typhus was sent. It came out to be positive for IgM ELISA (which is 86% sensitive). After that Doxycycline was added and the condition of the patient improved. Even though Scrub Typhus test was positive considering the clinical presentation and false positivity of scrub typhus in conditions such as Falciparum malaria, Pulmonary tuberculosis, Streptococcus viridians septicaemia and Typhoid fever. Diagnosis of Scrub typhus was non confirmatory. Enzyme levels repeated after 6 days ALT-54, AST-40, ALP-450, serum bilirubin came down to 3.7 with Direct bilirubin level of 2.0, Serum LDH was 631. USG (W/A) showed periportal cupping, suggestive of viral hepatitis with hepatomegaly & GB sludge. Lastly, noting the patient's history of recurrence of jaundice since age of 12 yrs, Hb typing was sent and it turned out to be HbS (homozygous). He also received 2 units of blood transfusion after that.

DISCUSSION :

In this paper we report one case of intrahepatic cholestasis which is rare but potentially fatal complication of sickle cell disease. Its etiology remains unknown, but it is believed that the deformed erythrocytes adhere to the hepatic vascular endothelium resulting in sludging and congestion of vascular beds, followed by tissue ischemia, infarction and liver dysfunction in the more severe cases. In the case described here the diagnosis of intrahepatic cholestasis was suspected because the sudden hyperbilirubinemia associated with a modest elevation of aminotransferases. Viral hepatitis can present a similar clinical feature, however elevated transferases is a frequent finding, sometimes with values higher than 1000 U/L. Furthermore, positive serology helps to define viral hepatitis. Another potentially confounding hepatic condition

is hepatic sequestration that present tender hepatomegaly associated with decrease in Hb concentration and reticulocytosis, a mild to moderate increase in aminotransferases, but not extreme hyperbilirubinemia. The so-called hepatic crisis is another hepatic condition considered in the differential diagnosis of SCIC. It is characterized by tender hepatomegaly, increasing jaundice, a mild to moderate elevation of aminotransferases, but the bilirubin concentration seldom exceeds 13 mg/dl. The case described here presented clinical features suggestive of SCIC and we performed aggressive conservative management and packed cell transfusions. The patient presented a favourable evolution and his hepatic function recovered to the previous pattern. Currently, the patient is maintained in a scheme of regular packed cell transfusion. So this case shows that intrahepatic cholestasis in the sickle cell anemia is benign and self-limiting condition.⁸

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A Rare Case of Dermato-myonecrosis & Acute Renal Failure Following Spider Bite

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Abstract

Of the > 30,000 recognized species of spiders, only about 100 are known to be aggressive and bite to defend themselves¹. The venom that the spiders use to immobilize and digest their prey can cause necrosis of skin and systemic toxicity. Whereas the bites of most spiders are painful but not harmful, envenomations by Recluse or fiddle spiders (*Loxosceles* species) and Widow spiders (*Latrodectus* species) may be life-threatening². *Loxosceles reclusa* envenomation may cause severe necrosis of skin & subcutaneous tissue with systemic hemolysis. There are Indian case reports of acute kidney injury with dermatomyonecrosis after *Loxosceles reclusa* envenomation³. Here we are reporting a case of severe necrosis of skin with multiorgan dysfunction following spider bite.

Key words: *dermatomyonecrosis, multiorgan dysfunction, envenomation.*

INTRODUCTION :

Spider bite is endemic in parts of North America, Mexico, tropical belt of Africa and Europe and can cause serious systemic toxicity.⁴ *Loxosceles* spiders belong to the family Loxoscelidae. Of the 13 species of *Loxosceles* identified 5 have been associated with necrotic arachnidism. *Loxosceles reclusa*, or brown recluse spider, is the spider most commonly responsible for this injury⁵. Dermonecrotic arachnidism refers to the local skin & tissue injury as a result of spider-bite. Loxoscelism is the term used to describe the systemic clinical syndrome caused by envenomation from the brown recluse spiders. The initial cutaneous lesion is that of an erythematous halo with edema around the bite site. This gradually gives way to vesicles & finally a dark brown necrotic ulcer. There may be hemolysis, renal failure and profound systemic reactions³. Although India is a home to a diverse array of arachnids, according to the latest updated lists of spider species found in India⁶, *Loxosceles rufescens* is the only

member of the *Loxosceles* genus described in India.

CASE REPORT :

A 17 year old unmarried Hindu male, Mr B. Tanti hailing from Meleng T.E Jorhat presented with gangrene involving right hand with pain abdomen and severe nausea and vomiting following spider bite 15 days back. Patient gave a history of spider bite over the dorsal aspect of right hand while he was working in his home. Initially he experienced burning sensation over his hand but later on he developed intense burning sensation all over his right hand and forearm. There was swelling with severe pain of the right hand and forearm developed after 1 day of the bite. He also complained of multiple episodes of vomiting for 1 day after the bite. He was admitted in local hospital where he was treated conservatively and his vomiting and burning sensation subsided but the swelling of right hand increased and he noticed blackening of the terminal digits initially and later on spreading over the whole right hand excluding the thumb. There was intense pain and tightness of the hand not relieved by analgesics. On the 3rd day of admission to hospital fasciotomy operation was done to relieve his pain. He was discharged against advice from the hospital to carry out regular dressing at home. However his general condition deteriorated at home and he developed severe pain abdomen, with nausea and vomiting

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at home which was persistent and continuous. On the 7th day after the bite he was taken to Jorhat missionary hospital where he received conservative treatment with wound dressing, i.v antibiotics and antiemetics

The condition of the patient didn't improve and he was



Fig 1 : Digital gangrene following spider bite.

referred to A.M.C.H, Dibrugarh on 25.3.15 & was admitted in dept of Medicine. On examination, patient looked seriously ill, pale looking, dehydrated with tachypnoea and respiratory difficulty without cyanosis. There was dry gangrene involving both surfaces of right hand & fingers with extension to distal fore arm. His B.P was 100/70 mmHg and pulse rate 110 BPM, regular. On abdominal examination, there was guarding and rigidity of the abdominal wall with decreased peristaltic sound without any organomegaly. Cardiovascular and nervous system examination were found to be normal. Wheeze was found on respiratory system examination. We carried out preliminary investigations where we got azotemia (urea 266mg/dl, creatinine 11.5 mg/dl), raised total count (T.C-14100, N82, L12, E4, M2), deranged liver function tests (total bilirubin-3 mg/dl, SGOT- 566U/L, SGPT-630U/L) with raised pancreatic enzymes (amylase 384 U, lipase 3361 U), USG whole abdomen revealed normal findings. Doppler study of upper limb vessels revealed normal study.

We started conservative management with IV fluids, antibiotics, liver support etc. We performed regular wound dressing in consultation with plastic surgery department and the patient also underwent 4 sessions of hemodialysis in consultation with nephrology department. Patients general condition improved after hemodialysis and his nausea and vomiting subsided. Routine blood examination, kidney function tests, liver function tests & amylase, lipase were repeated 5 days after admission and there were improvement of all the parameters. There was striking

clinical improvement of the patient after 1 week of treatment and serial estimation of biochemical tests revealed normalization of LFT, KFT & pancreatic enzymes. He was advised for amputation of hand by orthopedic dept but didn't give consent for that. We discharged the patient and asked him to attend plastic surgery and orthopedics dept for management of gangrenous hand.

DISCUSSIONS :

Acute intravascular hemolysis is a hallmark of loxoscelism. In our case, intravascular hemolysis was evidenced by low hemoglobin level with elevated unconjugated bilirubin and elevated LDH level. The likely etiology of renal failure in our case is hemolysis leading to acute tubular necrosis. Although the spider could not be seen, the features are typical of loxoscelism, specially the dermatomyonecrosis pattern of lesion with ARF. Most of the case series of Loxoscelism have documented dermatomyonecrosis with a few cases of hemolysis and rare cases of ARF. India belonging to the tropical country is home to several insects however many fatal spider envenomations go unreported in the absence of effective reporting system. It should be borne in mind that a case presenting with acute dermatonecrosis with other features of hemolysis or rhabdomyolysis or in rare instances acute renal failure could be due to Loxoscelism.

CONCLUSION :

Spider bite is not uncommon in this part (north-east) of our country due to its unique geographical distribution. Early recognition of the signs and symptoms along with prompt and appropriate timely intervention can save the life of the patient following spider bites which also play a pivotal role in preventing the fatal complications.

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Spontaneous Thrombosis of Splenic Artery Pseudoaneurysm Complicating Pancreatitis

A Dey* P Bhattacharjee** B K Nath***

Abstract

The natural history of pseudoaneurysms complicating pancreatitis is unknown. Pseudoaneurysm usually arises from the peripancreatic arteries or even the aorta, after arterial wall exposure to pancreatic enzymes and subsequent degeneration and hemorrhage.¹ Pseudo-aneurysmal bleeding is known to have very low incidence upto 10%.² The most common artery affected by pseudoaneurysm is splenic artery which is involved by almost half of the cases because of its contiguity with pancreas.² Once a pseudo-aneurysm has been identified, it should be treated whether or not it has caused bleeding.² Spontaneous pseudoaneurysm regression is a rare event. The spontaneous regression of a splenic artery pseudoaneurysm has, to our knowledge, been previously documented in only three case reports. Here we report on an unusual case of spontaneous thrombosis of a splenic artery pseudoaneurysm complicating chronic pancreatitis.

CASE REPORT :

A 17 year old male presented with pain abdomen for last 1(one) month with recent increase in severity since last 3-4 days associated with nausea and vomiting. The pain was boring, deep, epigastrically located and no association with eating or positional changes. He had history of similar episodes of pain (10-12 times) in the past from the age of 12 to 14yrs. There has been a recent change in the frequency of pain with one episode every 1-2 months. He had 2-3 episodes of bilious vomitus with nausea since last 2 days. A review of all the patient's body systems showed diarrhea, asthenia and weight loss (approximately 15 kg since his symptoms began). He is a non-smoker, non-ethanolic, had no history of such ailments running in the family. The patient had been taking hyoscine butylbromide, which provided only temporary relief of his abdominal pain. Although he visited many doctors in the past but had no valid past medical records with him.

On physical examination he had sweating and dehydration. His blood pressure was 90/70 mm Hg, pulse rate 110/min, respiratory rate 30/min. The abdomen was slightly distended, mild tenderness on palpation of the

mesogastric area and peristaltic sounds were sluggish.

Laboratory studies revealed the following(reference ranges shown parenthetically): total leukocyte count- $13.71 \times 10^3/\text{ul}$ (4000-11000/ul); erythrocytic sedimentation rate-90 mm AEFH (normal <15); urine routine examination was normal; serum sodium-137.6 mmol/l (136-146); serum potassium-4.42 (3.5-5.10); serum calcium-8.90 mg/dl (8.80-10.80); total bilirubin-0.24 mg/dl (0.30-1.20); random blood sugar-88mg/dl (80-140mg/dl); serum lipase-384U/l (1-67); serum amylase-190U/l (22-80).

A ultrasonography whole abdomen gave the impression of an Acute on chronic pancreatitis as evidenced by a borderline bulky in size pancreas with coarse and hypoechoic echotexture, a dilated splenic artery with whirlpool appearance suggestive of pseudoaneurysm.



Fig 1 :-USG (w/a) showing the dilated MPD

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Fig 2 : USG (W/A) showing the whirlpool appearance in the splenic artery lumen suggestive of aneurysm.

MPD was also mildly dilated in the neck region. The body region also showed intra-glandular cystic lesion of size 39×18mm.



Fig 3 : CT abdomen showing the pseudoaneurysm with intraluminal thrombus.



Fig 4 : CT abdomen of the patient showing dilatation of the main pancreatic duct.

A computed tomography scanning of the abdomen revealed mild fat stranding in tail region of pancreas, irregularly dilated MPD, dilated splenic artery with isodense intraluminal thrombus measuring 6.5cm × 5cm causing luminal narrowing, lumen measuring approx. 3cm × 2cm. There was also a loculated collection of approx. size 4cm × 2cm noted in the transverse mesocolon on left side which on post contrast study showed peripheral wall

enhancement, s/o pseudocyst formation.

MRCP of the patient revealed a saccular dilatation of the splenic artery with a lesion measuring 3.8cm × 3cm. The lesion showed a thick hypointense rim in T2 FS sequence with the lumen showing hyperintensity with post contrast enhancement in the lumen suggestive of partially thrombosed splenic artery pseudoaneurysm.

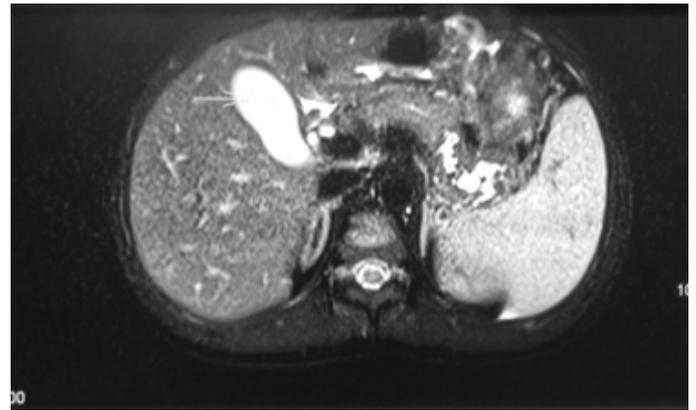


Fig 5 : MRCP of the patient showing the normal hepatobiliary system of the patient.

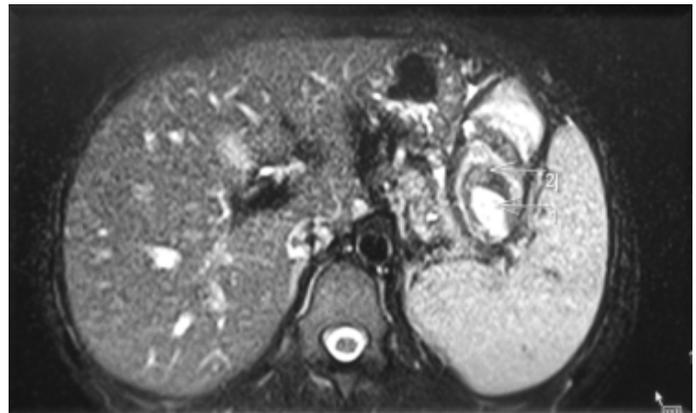


Fig 6 : MRCP of the patient showing splenic artery thrombus (2) with narrowed lumen(1).

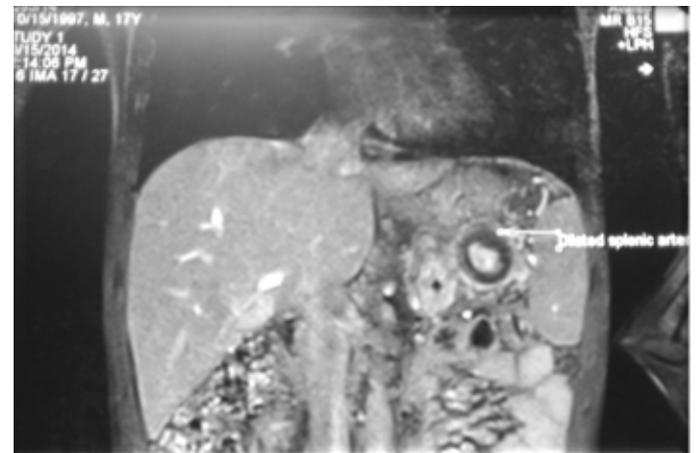


Fig 7 : MRCP image showing the dilated splenic artery with pseudoaneurysm.

The patient received fluids and electrolytes, hyoscine butylbromide, tramadol hydrochloride and pantoprazole. Nasogastric aspiration was done for a period of 2 days after which oral feeding was started once his pain and vomiting subsided. So this patient was finally diagnosed to be a case of acute chronic pancreatitis with an intraglandular cyst with a spontaneous thrombosis of a splenic artery pseudoaneurysm.

DISCUSSION :

Chronic pancreatitis is a disease process characterized by irreversible damage to the pancreas as distinct from the reversible changes noted in acute pancreatitis.³ The condition is best defined by the presence of histologic abnormalities, including chronic inflammation, fibrosis, and progressive destruction of both exocrine and eventually endocrine tissue.³ A number of etiologies may result in chronic pancreatitis, and may result in the cardinal complications of chronic pancreatitis such as abdominal pain, steatorrhea, weight loss, and diabetes mellitus.³ Patients with chronic pancreatitis seek medical attention predominantly because of two symptoms: abdominal pain or maldigestion and weight loss.³ The abdominal pain may be quite variable in location, severity, and frequency.³ The pain can be constant or intermittent with frequent pain-free intervals.³ Eating may exacerbate the pain, leading to a fear of eating with consequent weight loss.³ Pseudocysts occur in about 25% of patients with chronic pancreatitis and are most common in alcoholic chronic pancreatitis.² Pseudoaneurysms form as a consequence of enzymatic and pressure digestion of the muscular wall of an artery by a pseudocyst.² The pseudoaneurysm may rupture either into the pseudocyst (converting the pseudocyst into a larger pseudoaneurysm) or directly into an adjacent viscus, peritoneal cavity, or pancreatic duct.² Pseudo-aneurysmal bleeding may complicate 5% to 10% of all cases of chronic pancreatitis with pseudocysts, although pseudoaneurysms may be seen in up to 21% of patients with chronic pancreatitis undergoing angiography.² In our case, the patient reported abdominal pain without gastrointestinal bleeding; therefore, the pain was more likely associated with his initial pancreatitis process, rather than with the pseudoaneurysm itself. Once a pseudo-aneurysm has been identified, it should be treated whether or not it has caused bleeding.² Fortunately, the large pseudoaneurysm in this

patient thrombosed spontaneously instead of rupturing. To our knowledge, this unusual condition of a spontaneous thrombosis of a Splenic artery pseudoaneurysm secondary to pancreatitis is very rare. The causality and pathophysiology of this spontaneously thrombosed pseudoaneurysm is of interest.

Spontaneous regression of small visceral pseudoaneurysms has been reported.⁶ It is thought that a symptomatic visceral pseudoaneurysms smaller than 2.5 cm can regress spontaneously.⁷ Conservative treatment for this condition is recommended, except for women of child bearing age.^{8,9} However, the pseudoaneurysm was larger than 5 cm in our case. Factors that increase coagulability and decrease blood flow such as dehydration, hypotension, vasospasm, local damage to the arterial wall, and occult malignancy can cause spontaneous thrombosis of a pseudoaneurysm.¹⁰

Although the pathophysiology of spontaneous thrombosis in a pseudoaneurysm has been understood gradually and is still unclear. Visceral artery pseudoaneurysm should still be treated with transcatheter arterial embolization or surgical ligation if possible, because there is no definitive clinical evidence for predicting its outcome.

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A Case Report on Brachiocervical Inflammatory Myopathy

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Abstract

The myopathies are muscular disorders in which the primary symptom is muscle weakness due to dysfunction of muscle fiber.¹ This condition has widely varying etiologies including congenital or inherited, idiopathic, infections, metabolic, inflammatory, endocrine, and drug-induced or toxic.

Bibrachial palsy and the dangling-arm syndrome which is weakness, atrophy, and fasciculations of the hands, and shoulders characterize the common form of motor neuron disease, namely, amyotrophic lateral sclerosis. Primary diseases of muscle hardly ever weaken these parts disproportionately.

Key words : *Bibrachial palsy, The Dangling-arm syndrome.*

CASE REPORT :

A 27 years old man from Silcoori, Ghungoor, Silchar presented to our hospital with complains of weakness of both upper limbs for six months and difficulty in getting up from bed for one month which were gradual in onset and progressive in nature. He had progressive difficulty in combing his hairs which was followed by difficulty in holding objects with hands. Then he found difficulty in raising his head from pillow which was gradually progressing. At presentation he was totally unable to get up from bed on his own. Patient did not complain of any difficulty during micturition and defeacation. Patient was not addicted to alcohol and he had not taken any specific medicine earlier. Examination revealed atrophy of arm, forearm and hand muscles in both sides and also atrophy of supraspinatus, deltoid, trapezius, sternocleidomastoid bilaterally. Deep tendon reflexes were absent in upper limbs. Hypotonia was present in flexors and extensors of elbow and wrist joints on both sides and muscle power was 1/5 in flexors and extensors of elbow and wrist joints and 4/5 in trapezius and sternocleidomastoid muscles. All modalities of sensations were intact on examination and



Fig 1 : Picture shows atrophy of arm, forearm and hand muscles.



Fig 2 : Picture shows wasting of pectoral and neck muscles.

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fasciculation was absent. Investigations revealed haemoglobin 14g/dl, total leucocyte count 7340/ μ L, ESR 5mm AEFH, normal urine analysis report, serum sodium 135mmol/lit, potassium 3.81 mmol/lit, RBS 130 mg/dL, normal ECG, CSF analysis, normal serum protein electrophoresis report, normal nerve conduction study. ANA, HIV 1 and 2, HBsAg, antibodies against HCV were negative. MRI cervical spine revealed normal structure. CPK level was 652 IU/lit. Muscle biopsy showed moderate variation in size of fibres, interstitial inflammation, mononuclear cell infiltrate, fibre necrosis, regenerating fibres with large nuclei.

DISCUSSION :

Patients with brachiocervical inflammatory myopathy syndrome have progressive weakness in the proximal regions of the arms and neck. CPK level is moderately

elevated. The predominant histopathological findings are active myopathy, C5b-9 staining of endomysium, focal perivascular and perimysial inflammation³. In our patient, there was progressive weakness of upper limbs, neck, shoulder muscles, without any involvement of cranial nerve, facial and lower limb muscles. CPK was raised and muscle biopsy showed features of muscles fibre necrosis with mononuclear cell infiltration. We started steroid and patient was advised to come for follow up. Follow up examination after 2 weeks of discharge from hospital revealed significant improvement of muscle power.

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