ANALYSIS OF SURGICAL TREATMENT IN BRONCHIECTASIS -21 YEAR RETROSPECTIVE STUDY

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF M.Ch DEGREE (CARDIOTHORACIC SURGERY) EXAMINATION OF THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY, CHENNAI TO BE HELD IN AUGUST 2014.

CERTIFICATE

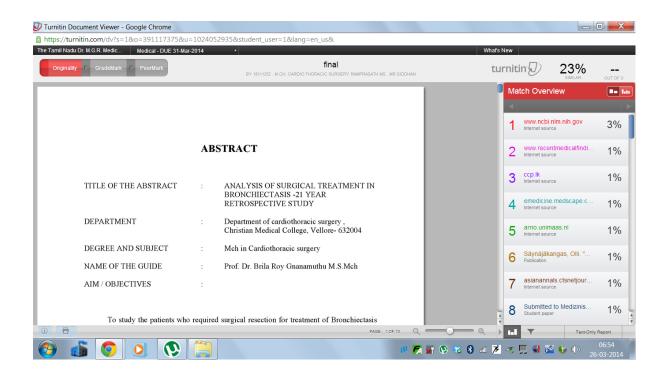
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Sub:

FLUID Research gra nt project:

Analysis of surgical treatment in bronchiectasis -21 year retrospective study.

Dr. M.S.Ramprasath., Senior PG Registrar, Cardiothoracic Surgery, Dr. Brila Roy Gnanamuthu, Cardiothoracic Surgery.

Ref: IRB Min. No. 8336 [RETRO] dated 18.06.2013

Dear Dr. M.S.Ramprasath,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Analysis of surgical treatment in bronchiectasis -21 year retrospective study." on June 18, 2013.

The Committees reviewed the following documents:

- 1. Format for application to IRB submission
- 2. Informed Consent Form and Patient Information Sheet (English and Tamil)
- 3. Cv's of Drs. Ramprasath, BrilaRoy Gnanamuthu
- 4. A CD containing documents 1 3

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The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on June 18, 2013 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

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We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be

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Yours sincerely

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ABSTRACT

TITLE OF THE ABSTRACT	:	ANALYSIS OF SURGICAL TREATMENT IN BRONCHIECTASIS -21 YEAR RETROSPECTIVE STUDY
DEPARTMENT	:	Department of cardiothoracic surgery, Christian Medical College, Vellore- 632004
DEGREE AND SUBJECT	:	Mch in Cardiothoracic surgery
NAME OF THE GUIDE	:	Prof. Dr. Brila Roy Gnanamuthu M.S.Mch
AIM / OBJECTIVES	:	

To study the patients who required surgical resection for treatment of Bronchiectasis in our institution over the last 21 years (1992-2012).

Demographic details, mode of presentation, investigations done, surgical details, morbidity, and mortality and long term surgical outcome are studied.

MATERIAL AND METHODS

We analyzed the patient details retrospectively using the charts as well as our clininical work station. Categorical data were expressed as frequency & percentage. Continuous variable expressed as mean \pm standard deviation or median and range. Significant differences between proportions determined by chi-squared analysis Or Fisher's

exact test. All analyses were carried out using Statistical Package for Social Sciences version 11.5 (SPSS, Inc., Chicago, IL, USA). Probability values p < 0.05 were considered significant

RESULTS

We had a total of 242 patients in our series from 1992-2012.Bronchiectasis is more common in males (64%). Commonly it involves left side. Patient opts for surgery because of failed medical treatment. Hemoptysis is the common indication (45%) for surgery. More than half (65%) of the patients have typical features of Bronchiectasis in the X-ray itself. HRCT was done before surgery for all patients, which is considered as the imaging of choice. Most of our patients had restrictive PFT (56%). Sputum had grown some organisms in 57% of our patients. Majority of our patients were operated for Hemoptysis (48%). Common procedure done for our patients was single Lobectomy (54.5%). There were 39 patients who had complications in our series. There was statistically significant association between pre-op cultures, preop PFT and extent of disease to the post operative outcome. Complete resection of the disease is single most important criteria for prevention of post-operative symptoms however bilateral diffuse disease shall remain to have post-op minimal symptoms. There were two mortality in our series.

CONCLUSIONS

Bronchiectasis is primarily a medical disease which requires careful assessment and diagnosis. Once diagnosis is made, the patient should be under medical surveillance and treatment for repeated infections and haemoptysis. Appropriate antibiotics as dictated by

cultures should be initiated in order to avoid progression of the disease. If and when surgery is indicated, a thorough pre-operative evaluation should be carried out. As in other literature, our study also proves that surgical treatment for Bronchiectasis can be done safely with minimal acceptable mortality and morbidity. Single most important factor which decides on the symptom free state after surgery is the adequacy of the resection. Complete resection of the localised Bronchiectasis offers better cure as well as symptom free survival after surgery. However it should be appreciated that in cases of diffuse bilateral disease, post operative residual Bronchiectasis is unavoidable. In such cases, though the intensity of symptoms may improve greatly after surgery, minimal symptoms may persist.

Key words

Bronchiectasis surgical management, post-operative complication, residual Bronchiectasis.

INTRODUCTION

Bronchiectasis is chronic respiratory disease which has a got long duration of symptoms, varied clinical presentation and numerous methods of management. It is primarily a medical disease which requires careful follow up, once the medical treatment becomes ineffective the patient is offered surgical treatment. The exact incidence of this disease is difficult to estimate because most of the studies in the literature are based on radiological investigations and treatment was offered to the patient coming to hospital. The burden of this disease in the community level especially in developing countries is more than the estimated figure. The surgical treatment for Bronchiectasis in the previous era was pneumonectomy, but the concept of lung parenchymal preservation lead to lobectomies. The various procedures for Bronchiectasis includes lobectomy, bilobectomy, segmentectomy alone or together with lobectomy and pneumonectomy. The surgical treatment in Bronchiectasis can be safely performed with acceptable morbidity and mortality.

AIMS

To study the patients who required surgical resection for treatment of Bronchiectasis in our institution over the last 21 years (1992-2012).

Demographic details, mode of presentation, investigations done, surgical details, morbidity, and mortality and long term surgical outcome are studied.

OBJECTIVES

The objective of our study was to analyse the patient demographics ,mode of presentation, investigation, type of surgery performed in relation to post-operative outcome in terms of complete relief of symptoms or persistence of minimal symptoms.

MATERIALS AND METHODS

The records of all patients who underwent surgical treatment for Bronchiectasis at our institution between January 1992 and December 2012 were retrieved. The demographic details of the patient, the mode of presentation, indication for surgery, pre-operative investigations like sputum culture , X-ray, Computerised Tomography, type of surgery offered, post operative complications, follow up of the patient were studied in detail.

Statistical analysis of the data was performed using the chi- square test, paired T test, frequency and percentages. All p-values were two tailed and a value of less than 0.05 was considered significant.

SURGICAL TECHNIQUE

All patients received prophylactic antibiotics of Inj. Ceftazidime 30-50 mg/kg/day and Inj. Augumentin 15 mg/kg at the time of induction and followed by Inj. Ceftazidime 30-50 mg/kg/day in divided doses for two more days and oral Augumentin 25mg/kg for 5 days. All the patients were subjected to Double lumen Tube (DLT) intubation for favour of isolation of the lung. A standard posterolateral thoracotomy with or without cutting serratus anterior muscle was performed for all cases. After the desired procedure patients were extubated on table and shifted to post-operative ward. After single day observation patients are transferred to ward unless warranted.

FOLLOW UP

Retrospective analysis of the hospital records were used to study the follow up data of patients . During the follow up period the symptoms were analysed, X ray was taken as a routine for all patients who come for follow up. In patient who were symptomatic High resolution Computerised Tomography was taken.

REVIEW OF LITERATURE

Definition of Bronchiectasis

Bronchiectasis (bronchus-tube, ectasis-to stretch) is a chronic respiratory condition which is characterized by abnormal permanent dilation of the bronchi. Bronchiectasis, as described Reid in 1999 as a permanent dilatation of bronchi with destruction of bronchial wall, holds good even today. It is caused by destruction of the elastic and muscular components of the bronchial walls. With the advent of antibiotics the incidence of Bronchiectasis has declined in developed nations, but in developing countries it still causes significant morbidity and mortality (1). Ironically, even in a well developed country like USA the burden of the disease is steadily increasing in the current decade when compared to the earlier decades(2).

Epidemiology

It is not easy to estimate the prevalence of this disease in any particular geographical area in the past, since most of the literatures in the earlier times were based on chest X-ray findings only. Chest x-rays is not the most sensitive tool for diagnosing Bronchiectasis.

With the evolution of High Resolution Computed Tomography (HRCT) it is observed that even in persons undergoing investigation for unrelated respiratory diseases like Chronic Obstructive Pulmonary disease (COPD) and bronchial asthma and even in smokers with chronic bronchitis there is incidental diagnosis of Bronchiectasis, hence it's obvious that the prevalence of the disease tends to be underestimated.

Certain ethnic groups like native North Americans, Western and Maoris of New Zealand have high incidence of the disease either due to genetic factors or due to environmental factors. The exact prevalence in a population can only be obtained with the availability of a cheap, widely applicable yet accurate imaging technique.

Types of Bronchiectasis

1. Cystic or saccular type

Bronchial wall is dilated like balloon.

Usually seen in children due to repeated viral or bacterial infection.

2. Cylindrical type

Cylindrical dilatation due to lesser degree of damage.

It is often diffuse and affects lower lobes commonly

3. Varicose type

Areas of stenosis and constrictions in dilated bronchi

4. Traction Bronchiectasis

Usually occurs in setting of pulmonary fibrosis.

Fibrosis causes traction on the bronchial wall.

Aetiology

There are numerous known causes of Bronchiectasis, yet in half of the patient the cause may not be known. Bronchiectasis may be congenital or acquired. In congenital Bronchiectasis, the bronchial tree is diffusely involved, whereas when acquired due to infection, it tends to be localized. The following causes, adapted from Barker et al(3) summarizes the various etiologic factors for Bronchiectasis.

The underlying common mechanism for development of Bronchiectasis is recurrent, transmural infection and inflammation of the bronchial wall.

Aetiology

Congenital causes Acquired causes Infections Inhalation of toxins Foreign body aspiration

Connective tissue disorders

Infection

Bronchiectasis can be caused by bacterial, viral or fungal infections. Repeated infections destroy the wall of the bronchus causing the disease. Bronchiectasis in childhood used to be a common complication of measles or pertussis in the past, but effective vaccination has decreased the prevalence of the disease even in developing countries.

Currently, adeno and influenza viruses are associated with the development of Bronchiectasis in children. Organisms like S. *aureus, K.pneumoniae, H. influenzae,* and anaerobes are also important causes of Bronchiectasis. It is an interesting observation that whenever appropriate antibiotic treatment is delayed or deferred while treating the common causative pathogens of Bronchiectasis, there is a propensity for the same bronchi to be by repeated infection which ultimately leads to Bronchiectasis of that area.

In 64% of patients with Bronchiectasis there is presence of potentially pathogenic bacteria (PPM). Common PPMs include *H. influenzae, Pseudomonas* spp, and *S. Pneumonia.* Varicose or saccular Bronchiectasis are risk factors for such colonisations(3). Human immune deficiency virus (HIV) affected patients in their later stages develop Bronchiectasis due to repeated infections.

Tuberculosis (TB) remains an important cause of Bronchiectasis in underdeveloped countries. In developing countries tuberculosis is endemic. Together with poor hygiene and

overcrowding it is a major cause of cause of Bronchiectasis(4). The prognosis becomes worse if atypical Mycobacterium are involved.

Mechanical obstructive causes

The obstruction to the bronchi can be either intra luminal or extra luminal. Main causes for intra luminal obstruction are foreign bodies and neoplasm. Extrinsic compression is usually due to enlarged lymph nodes around the bronchi. The mechanisms for development of Bronchiectasis are

- 1. Impaired clearance of the secretions resulting in repeated infections leading to damage to bronchial wall
- 2. The negative intra pleural pressure along with atelectasis causes centripetal pull on the bronchial wall

In extremes of age, aspirations of foreign body often go unnoticed for a long time till symptoms develop (5).

Congenital causes

Impaired mucociliary clearance

Cystic fibrosis

Cystic fibrosis (CF) is caused by a mutation. CF is caused whenever there is mutation in the gene cystic fibrosis trans membrane conductance regulator. It usually involves both the upper lobes. The thick secretions in cystic fibrosis interfere with effective mucociliary clearance thus making the individual prone for recurrent infections leading to Bronchiectasis. They often develop opportunistic infections, usually pseudomonas aeruginosa which becomes chronic and makes the individual prone for Bronchiectasis(6). Milder mutations of cystic fibrosis may present as late onset Bronchiectasis.

Primary ciliary dyskinesia

Primary ciliary dyskinesia is an autosomal recessive disorder, here the cilia have ultra structural abnormalities. Abnormal micro tubules, absence of one or both dyenin arms, abnormal radial spokes are the common abnormalities making the cilia immotile, or beat in disorderly fashion, thereby hampering mucus clearance.

Ciliary dysmotility syndromes

Here the cilia are dyskinetic and hence the muco-propulsive action is decreased leading to impairment in clearing secretions favouring bacterial colonization, eventually leading to infection and subsequent Bronchiectasis. There are associated syndromes like Kartagener's which includes recurrent respiratory tract infections, sinusitis, otitis media, bronchiectasis, situs inversus and immotile sperm(7).

Immune deficiency

Congenital impairment in immune mechanisms is another important cause of Bronchiectasis as seen with immunoglobulin deficiencies including panhypogamma globulinemia, IgG subclass deficiency and selective IgA deficiency (7). Immune mechanisms should be suspected in patients with recurrent acute episodes rather than chronic infection. IgA deficiency occurs in 0.1%-0.2% of general population. IgG subclass deficiency like IgG2 is associated with recurrent pneumococcus pneumonia. An acquired immunodeficient state is noted in individuals suffering from lymphoma, leukaemia and multiple myeloma. In such patients, recurrent infections can lead to cylindrical Bronchiectasis.

Non-infective- inflammatory causes

Inhalation of toxic gases such as ammonia, chlorine or smoke can cause the inflammation in bronchial mucosa. It basically causes obliterative bronchiolitis. This, together with damage to the walls of the larger bronchi can cause cylindrical Bronchiectasis. Aspiration of gastric contents triggers severe inflammatory responses leading to bronchial wall destruction leading to Bronchiectasis.

Immune mediated causes

In allergic bronchopulmonary aspergillosis, there is an immune response to colonized *Aspergillus* organisms which in association with asthma can lead to cylindrical Bronchiectasis (8).

Bronchiectasis can also occur in other immunologic diseases like ulcerative colitis(9), rheumatoid arthritis and Sjogren's syndrome. Alpha 1 Antitrypsin, deficiency, in which early onset and severe pan-acinar emphysema is the usual manifestation, may also be accompanied by Bronchiectasis (10).

Alpha-1 antitrypsin deficiency is associated with increased incidence of chronic obstructive pulmonary disease (COPD) and Bronchiectasis (11).

Non tuberculous Mycobacterium (NTM) and Bronchiectasis

Mycobacterium Avium intracellulare complex and mycobacterium kansasii are known to cause progressive Bronchiectasis that is limited to middle lobe and lingula. It typically involves healthy, non-smoking, thinly built women resulting in the so called Lady Windermere syndrome (12).

Pulmonary fibrosis

Fibrosis of due to causes like sarcoidosis, radiation, cryptogenic fibrosing alveolitis could also lead to Bronchiectasis.

Pathophysiology

Cole's "vicious cycle hypothesis" says that environmental insult with genetic susceptibility combined with decreased muco-ciliary clearance results in persisting microbes in the sinobronchial tree and microbial colonization, results in tissue damage and decreased mucociliary motility. This leads to more infection with a cycle of progressive inflammation causing lung damage. The current view is that the two factors required for the development of this condition are persistent infection and a defect in host defence(13).

The inflammatory changes in the walls of bronchi in medium-sized airways lead to the destruction of normal structural components of the wall, including cartilage, muscle, and elastic tissue, which are replaced by fibrous tissue. Bronchial wall is destroyed by proteases released predominantly by neutrophils, which damages large airways leading to bronchial dilatation(14). Finally the inflammation spreads beyond airways to cause interstitial pneumonia. Recent investigations have also proved that lymphoid aggregates in chronic obstructive pulmonary disease (COPD) patients also cause bronchial thickening (15). As with other infections, dominant cells of inflammation in Bronchiectasis are neutrophils, macrophages and lymphocytes. Neutrophils are the main source of proteases (16). Adjacent parenchyma is also involved in the inflammation and may lead to localized emphysema(17). The dilated airways are commonly filled with pools of thick, purulent material and more distal airways are often occluded by secretions or obliterated by fibrous tissue. The parenchyma that is supplied by the affected airways is commonly abnormal, with varying amounts of fibrosis, emphysema, pneumonia, and atelectasis. As a result of this inflammation there is enhanced vascularity of the bronchial wall with enlargement of the bronchial arteries and abnormal anastomosis between bronchial and pulmonary arterial circulations. This is the principal source for haemoptysis in such patients which may require urgent angiographic or surgical intervention.

Distribution of Bronchiectasis

Infectious causes tend to affect the upper lobes if secondary to tuberculosis while the other bacterial or viral pathogens affect lower lobe. The lower lobes are more affected due to retention of secretions in the dependant portion of the lungs(18,19). Middle lobe gets affected by the disease because of its long slender bronchi with acute angulations which gets easily compressed by a collar of enlarged lymph nodes(20–24).

Malnutrition and socio-economic status

Bronchiectasis is a major problem in developing nations like India(25), china(26), turkey(27), Hong Kong and in certain parts of south America(28). Even in certain subset of immigrants in developed countries it is common. Malnutrition is associated with lowered immunity which may explain the increased prevalence in such groups.

Extremes of age

The immune system in childhood as well as old age seems to be less effective making these individuals more prone for development of the disease. Childhood infections especially during first few years of life with persistent infection during childhood make them susceptible for development of Bronchiectasis. In old age there is increase the incidence of COPD and subsequent development of Bronchiectasis because of repeated chronic infections.

Microbiology

The nature of bacterial flora in Bronchiectasis varies depending upon the location, severity of disease and duration. Studies have shown that *H.influenza* followed *by Pseudomonas aeuroginosa* as common organisms (29–31) isolated from Bronchiectasis patients. Appearance of sputum and the growth of microorganisms from it is misleading, as the most purulent appearing sputum may not grow any organism(32–35). The bacteria also changes its strains once in every two or three months in chronic patients(36). In COPD patients its noted that during the time of acute exacerbations the bacterial flora changes (37). Likewise in Bronchiectasis, depending on the severity of disease, the bacterial flora changes constantly (35).

H.influenza followed by Pseudomonas are the most commonly isolated organisms. *H.influenza* which is isolated has varying types depending on the geographical area. These non tuberculous micro-organisms may complicate the outcome of the patient depending on the immunity of the patient (38,39).

Role of viral involvement in Bronchiectasis is not well dassociated unlike in COPD(40). However, some investigators have consistently isolated adenovirus in children with Bronchiectasis(41).

Effects of bacterial pathogens on the respiratory tract

The bacterial colonies in the respiratory tract have direct as well as indirect effect by lowering the host immune response leading to damage in the ciliary epithelium. In chronic cases, this bacterial enzymatic reaction damages the bronchial wall, attracts the neutrophils which causes further damage to the epithelium, cartilage and lung parenchyma resulting in permanent structural damage. Certain organisms like *H.influenza* directly invade the parenchyma (42,43),whereas pseudomonas has the capacity of form a bio film around itself to help escape from immune mediated cells(44).

Clinical features

Patients with Bronchiectasis present with recurrent pulmonary infections manifesting from no symptoms to simple cough with expectoration and dyspnoea. Some patients have unremitting chronic cough with thick, tenacious purulent sputum. Haemoptysis is a common symptom with which patient may be hospitalised. It may range from streaks of blood to massive haemoptysis requiring urgent intervention(45). In many studies in the third world as well as in developing countries, Bronchiectasis remains at the top of the list as a cause for haemoptysis(46–48). The source of bleeding is from the dilated tortuous peribronchial arteries of the affected region which erodes into lumen causing haemoptysis. Auscultation reveals crackles, wheeze, rhonchi or signs of bronchospasm. Haemoptysis may be life threatening if source of bleeding is from the neo-vascularizied vessel which usually is stimulated by hypoxia and chronic airway inflammation(49,50). It is common in India where patients with Bronchiectasis will be having productive cough for a long time. After taking "over the counter" drugs for considerable time, they present to hospital only if there is haemoptysis. Since inception, bronchial artery embolization has saved many patients from catastrophe. Initially, spongicel was used, but this had significant incidences of rebleed (51). Later, the use of coils for embolization has made dramatic improvement since the recannalisation rates are low (52). The bronchial arteries when it dilates due to hypoxiemia of that region tends to develop anastamosis with pulmonary arterioles thus giving rise to left to right shunt. In extreme cases, there may be features of pulmonary artery hypertension when there is excessive left to right shunting(53).

Diagnosis

Any patient who presents with chronic muco-purulent sputum must be worked up for Bronchiectasis (54). If patients are educated to measure the sputum volume every day, interestingly it has co-relation with quality of life and lung function (55). Non-specific symptoms like malaise, fatigue, evening rise of temperature, chest pain, breathlessness on exertion may be present(54,56,57). Haemoptysis is an important symptom which the patient really worries and seeks medical attention in developing countries(58). Certain physical findings like crackles , wheeze and clubbing of digits may be present in some patients(54,56).

A plain chest X-ray will give the diagnosis of Bronchiectasis if it is severe enough and shows classical honey-comb pattern(59). There is a problem of under diagnosis with these x-ray studies. It has been demonstrated in many studies that it can diagnose only 50% of the cases, remaining patients require additional investigations to confirm the pathology(60). Tram lines or parallel lines seen along the course of bronchi in a plain chest X-ray indicate severe Bronchiectasis. Before the era of CT scan, bronchography was used to confirm the diagnosis. After the availability of Computerised tomography this has become the gold standard in diagnosing Bronchiectasis especially the High Resolution Computed Tomography (HRCT) (55,61). Cystic type of Bronchiectasis gives shows multiple air fluid levels. In cylindrical variety the dilatation appears smooth and more uniform. Varicose type usually little advanced type with uniform dilatation alternating with areas of constriction giving a beaded appearance.

In HRCT, the thorax is scanned twice, once during suspended inhalation and another during exhalation to detect minute details and micro air trapping. Certain features in HRCT are almost diagnostic of the condition like:

- Signet ring formation where diameter of bronchi appears more than adjacent pulmonary arter
- 2) Absent normal tapering of the bronchi
- 3) Unusual appearance of bronchi at the periphery (54,56,62).

The findings of the HRCT is important as it has been proved in studies that it corelates with clinical outcomes (54,61,63). Mucus plugging along with dilated arteriole and aggregates of nodule appear like tree-bud in CT. With the new technological advances like multi detector computed tomography, it is possible to reconstruct with 3-Dimensional imaging and asses the airway in a better way(64,65). Pulmonary function testing in these cases is useful in diagnosing the air flow limitation, but it does not help to identify the early structural damage. FEV1 is usually low in patients when there is considerable damage to the parenchyma of the lung.

Bronchoscopy may be diagnostic or therpeutic. It can diagnose a bronchostenosis and help in retrieving a foreign body to clear the airway. In cases of acute on chronic exacerbation, it can be used to obtain cultures for planning appropriate antibiotics. Broncho alveolar lavage helps in decreasing the bacterial load thus helping chronic patients who suddenly worsen (66).

Diagnosis is arrived with proper history with HRCT and spirometry. Co-existent symptoms and age of presentation decides the necessity of further work-up like sweat-chloride test to rule out cystic fibrosis, serum immunoglobulin, perciptin antibody, or electron microscopy to look for ciliary related problems(67).

Management

There are myriad of management for Bronchiectasis but the ultimate goal of treatment should aim the following

- 1) To limit the cycle of infection
- 2) Prevent airway damage
- 3) Improve symptomatology
- 4) Reduce the exacerbations

5) Improve quality of life (54,57)

General supportive care

General health measures like maintaining good nutrition, avoiding smoking, regular exercises and breathing fresh air are considered general supportive measures for any pulmonary ailment patients(68). Management of this condition ideally should be team work including the physician ,thoracic surgeon, physiotherapist ,psychologist ,nurses and occupational therapist (68). However there is no definite management protocol and it has to be tailored according to the individual patients.

Management of underlying causes underlying causes

Next step in the management is to identify the underlying treatable cause for the disease. Studies have shown that even if the underlying cause is identified it may not alter the natural history of the disease (54).

Methods to prevent secondary infection

It is evident that in Bronchiectasis repeated infections play a vital role in the pathogenesis. In order to prevent the secondary infections especially in childhood appropriate vaccination may be used .There is no data in favour or against the Influenza vaccination in both child and adult patients. But general concept of this vaccination is that it will help in preventing the acute exacerbations induced by this organism (59). In the same way, for the

23-valent pneumococcal vaccine also, studies and extensive Cochrane database review concluded that there is no added advantage of vaccination. However, the general concept is to administer this vaccine for both adult and children even if the advantage is minimal(69).

Mobilisation of bronchial secretions

It forms important part in the medical management as well as pre-operative preparation of the patients as it breaks the vicious cycle of the disease. Commonly used therapy techniques are:

1) High frequency percussion

2) Positive expiratory pressures

3) Active cycle of breathing exercises

4) Postural drainage.

All these exercises not only train the muscles but also help in increasing exercise capacity and in turn improve quality of life (70).

Bronchodilators

Although there is varying degree of airflow obstruction with airway hyper reactivity, bronchodilators are very useful. Many studies are conducted in the past to find the effects of short-acting or long-acting beta-agonists, methylxanthines or short-acting anticholinergics in the management of patients with Bronchiectasis(54,56,71–73).

Antibiotics

Various studies has proven the usefulness of antibiotics during acute infective exacerbations and during the maintenance phase(70). The route of administration should be individualised to patient as either oral, parentral or inhalational. The choice of antibiotics should be directed by the sputum culture report. Generally, common organisms like *P aeruginosa*, *H influenzae*, and *S aureus respond to* broad spectrum antibiotics. (74). Intravenous antibiotics should be reserved for sicker patients who are not responding to oral therapy.

In one study, a 14-day course of intravenous antibiotics improved systemic symptoms, sputum volume, bacterial clearance, inflammatory markers and quality of life but not the pulmonary function as indicated by FEV1 and FVC)(75). There is also substantial evidence in literature on the use of prolonged antibiotics in patients with Bronchiectasis, in particular with severe bronchial sepsis, and in cases not responding to conventional courses of antibiotics which show meagre benefit with regard to symptoms, improved sputum parameters, decrease in inflammation, and improvement in lung function. Hence it is recommended that if long-term antibiotics are to be used in Bronchiectasis, it should be confined to the subset of patients with chronic bronchial sepsis who are not responding to conventional antibiotic therapy or in cases with frequent exacerbations. There is however, emerging evidence in support of long-term macrolide therapy in patients with Bronchiectasis not responding to the usual regimen. Inhaled antibiotics for Bronchiectasis was investigated

extensively, especially for pseudomonas infection with tobramycin and gentamycin, but it was found out that it is successful in reducing the bacterial density only.

Anti-inflammatory treatment

After extensive research, the two drugs considered important in the treatment of in Bronchiectasis are:

1) Corticosteroids

2) Macrolide antibiotics

Corticosteroids

It is used in patients with Bronchiectasis associated asthma, COPD, or airway hyper reactivity. Many studies indicate that their primary anti-inflammatory action is beneficial in the treatment of Bronchiectasis(76,77). Though short term benefits are noted with high dose inhaled steroids, recent Cochrane review suggests that use of inhaled steroids either routinely or during exacerbations is not recommended(**7**8).

Macrolides antiobiotics

Macrolides reduces airway infection and inflammation. Thus it reduces the volume of sputum and release of inflammatory markers as well. Its mechanism of action is multifactorial extending beyond its antimicrobial action. It has been identified to exert its action on the immune system making the host more sensitized to other pathogens. However there is not much improvement in the overall quality of life (79). They also have significant effect on mucociliary clearance which helps in clearing of the sputum (81).

Macrolide resistance is known and is more common in patients who have infection by Mycobacterium avium complex(80).

Surgical management of Bronchiectasis

In the past, surgical therapy was cornerstone in treating focal Bronchiectasis. In modern antibiotic era with effective drug therapy and supportive treatment, ,surgery has become much less common (81). However, patients with refractory symptoms in spite of excellent medical management may benefit from resection of a localized bronchiectatic segment or lobe. Before embarking on surgery, a uncorrectable predisposing factor like ciliary dysmotility should be excluded especially in patients with multifocal disease.

The CT scan should be critically reviewed and other supportive investigations should be reconfirmed before making a final decision about resection to ensure that there is no multifocal involvement. The surgery is planned to preserve as much normal Parenchyma as possible at the same time not to retain potentially infective foci of parenchyma which will make the patient symptomatic soon after an incomplete resection.

There are studies to prove that lung resection is beneficial in Bronchiectasis both in children as well as in adults. Aggressive medical and physical therapy are recommended before surgery is contemplated.

Specific indications for surgery are:

(1) Haemoptysis –recurrent episodes of small bouts or single life threatening episode ,(2) Localized disease which doesn't respond to medical treatment

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- (3) Persisting symptoms
- (4) Resectable disease causing persistent foci of infection
- (5) Resectable disease with failure to thrive.

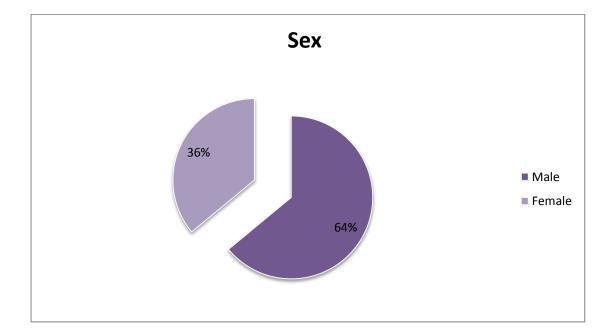
Although there are numerous studies published comparing the clinical experience with various surgical techniques in the management of Bronchiectasis it is the decision of the individual thoracic surgeon to decide about the operability and to redefine the indications according to the patient's need(81–87). The Cochrane review indicated that there were no randomized or controlled trials which compares surgery with nonsurgical treatment for Bronchiectasis (88).

Until 1970's physicians believed bilateral or multi segmental Bronchiectasis was considered as contraindication for surgical treatment (89) due to the poor results (90).. After 1970, the thoracic surgeons came up with the concept that bilateral disease is not a contraindication for surgery since the results had increased. (90). Surgery should be reserved for patients in whom curative resection can be achieved and these are usually cases of localized cystic unilateral Bronchiectasis. The indication can also be extended to bilateral localized Bronchiectasis or completely destroyed lungs provided the residual respiratory function is good. Resection of localized cystic bronchiectasis in the presence of scattered cylindrical bronchiectasis can improve symptoms and quality of life with low operative morbidity.

Surgical intervention is considered in patients with massive haemoptysis that originates from hypertrophied bronchial arteries. However, it is necessary to recognize that surgical resection should be considered only in a patient with sufficient pulmonary reserve. Embolization of bronchial artery, even with its high rates of recurrence, is an excellent alternative tool for emergency surgery for massive haemoptysis now a days.. The surgical technique for resection is difficult to standardize but the ultimate goal for the surgeon should be, to preserve as much as lung possible. Lung Transplantation is an option for patients who are seriously compromised in pulmonary function and chronic respiratory failure.

Results and Observation

In our study there were 242 patients out of which 155 (64%) are male remaining 87(36%) were female.



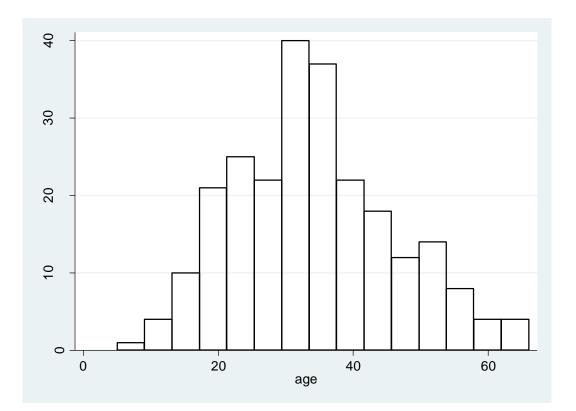
AGE

The mean age of presentation for surgery is 34 years, youngest was 12 years old and the oldest 66 years.

Table-1

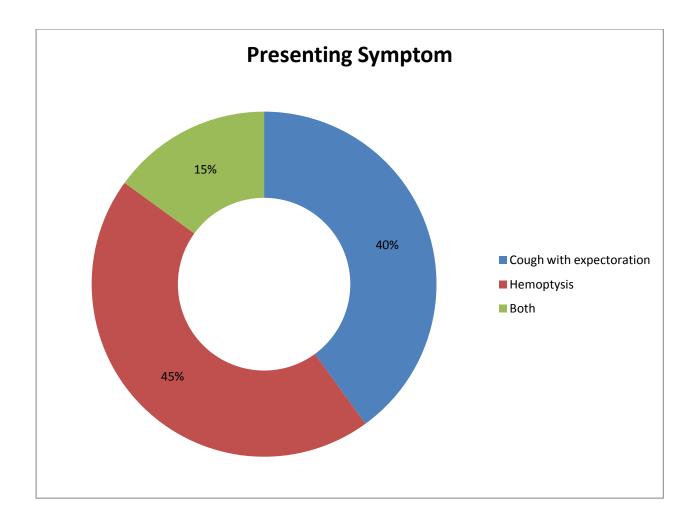
Variable	n	Mean	S.D.	Minimum	Median	Maximum
Age	241	34.19	11.83	12	33	66

It is observed that majority of our patients belong to second and third decade of life.



Presenting symptoms

The most common complaint at presentation was Haemoptysis (45%) followed by copious expectorations (40%). Fifteen percentage of them had both symptoms.



Duration of symptoms

The average duration of symptoms at presentation was 5.5 years . The duration of symptoms ranged from 1 month to 34 years.

Distribution of the disease

It is found that majority of the patients had Bronchiectasis on the left side 56%, 33% had disease only on right side. About 11 % of patients had bilateral disease. Most patients had bilateral minor disease as evident in HRCT.

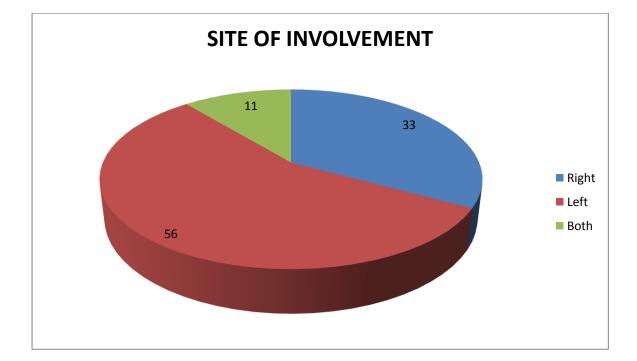
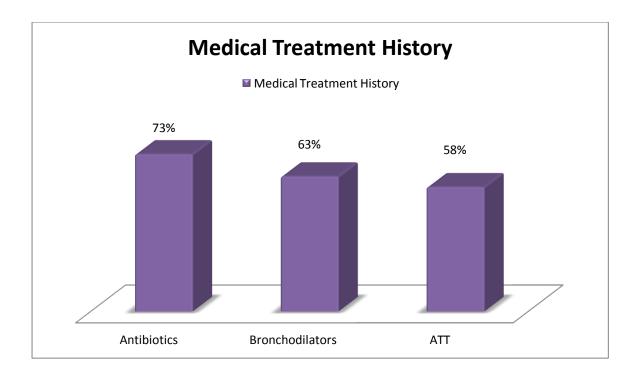


Figure -4

Medical treatment history

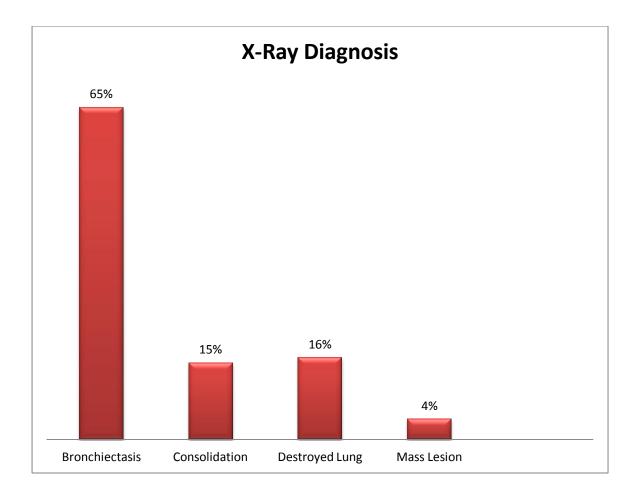
Seventy three percentage of percentage the patients had been treated with short or long term antibiotics repeatedly, 63% of them were on oral or inhaled bronchodilators along with antibiotics. Nearly 58% of the people had taken anti-tuberculous treatment (ATT).



The average duration of medical treatment before being referred for surgery is 4 years in our series.

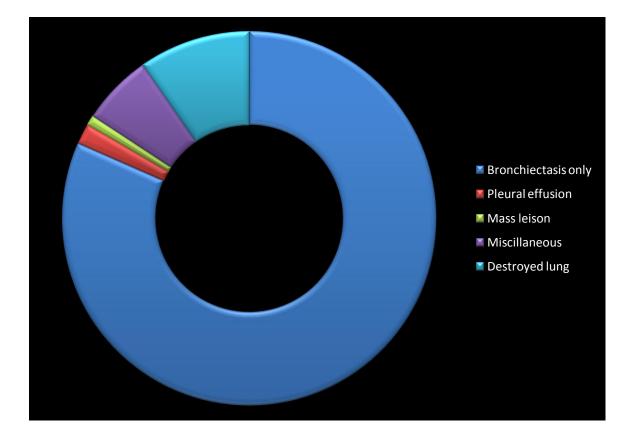
Investigations

All the patients in our series underwent chest x-ray and in 65% of the patients, the diagnosis was made with just the x-ray.



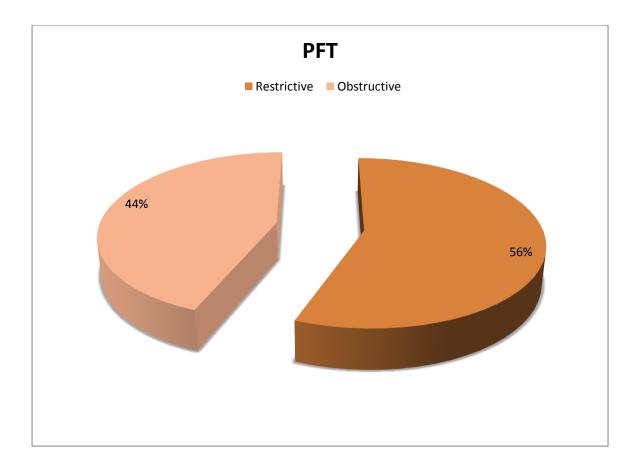
High Resolution Computed tomography (HRCT) findings

HRCT showed features favouring Bronchiectasis only in 93% of patients. It is also helpful in identifying completely destroyed lungs (11%), pleural effusion (2%), unrelated mass lesions (1%) and miscellaneous findings in 7% of patients.



Pulmonary function test (PFT)

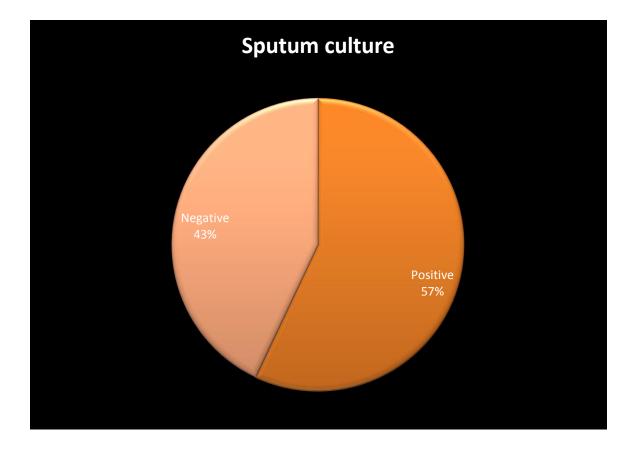
PFT was done in all patients prior to surgery. In 56% of patients it is restrictive and the remaining 44% it showed obstructive pattern.



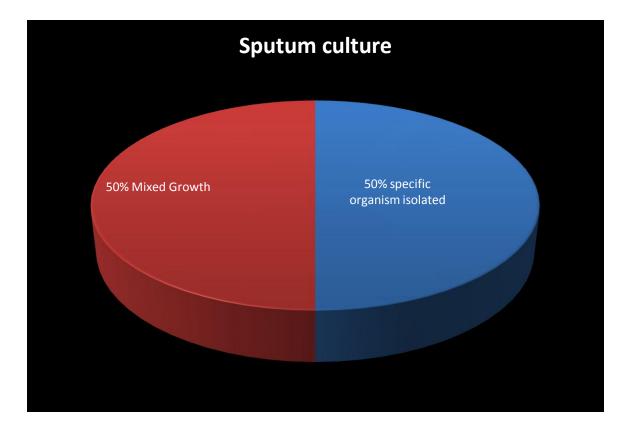
The average FEV1 in our series is 1.96L, FEV1/FVC ratio is 87.5%. Most of our patients had restrictive pulmonary function test.

Sputum culture

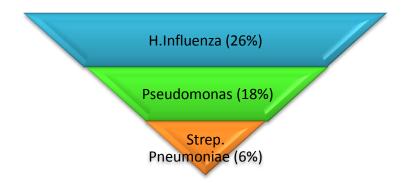
Sputum was positive in 57% of the patients only.



A mixture of organisms were seen in half the patients. Hemophilus influenza was isolated in 26% of them, Pseudomonas species in 18% and Strep.pneumoniae in the rest.



Split up of specific organisms isolated



Bronchoscopy

All the patients were subjected to bronchoscopy. 12 patients (0.05%) were identified to have significant bronchial stenosis. Seven of the setenosis were on the left and five were on the right side.

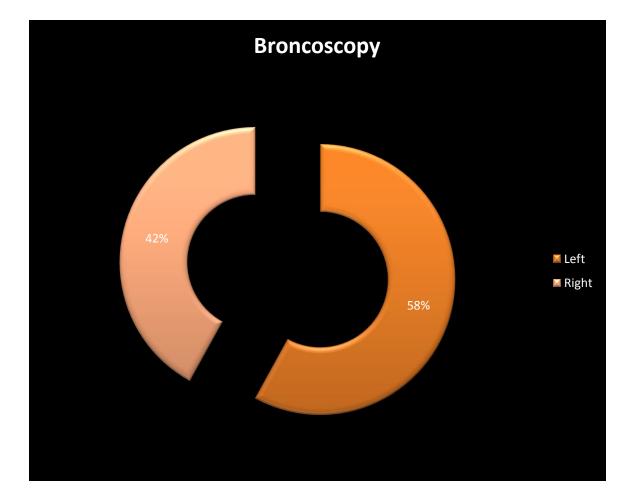


Figure-11

Indications for surgery

The most common indication was haemotpysis in 48% then cough with copious expectoration in 46% of patients, both in 13% of the patients.

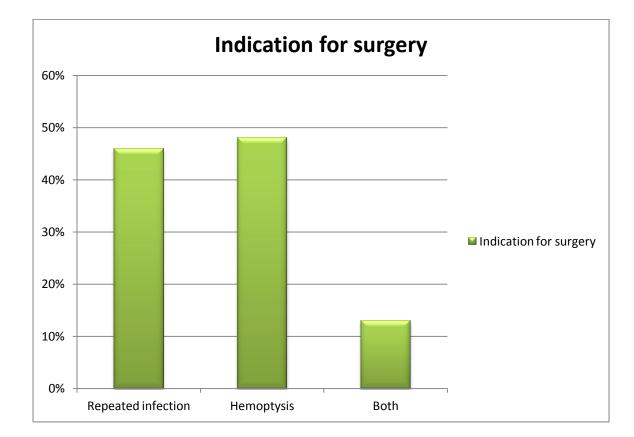


Figure-12

2% of our patients (5 patients) had undergone previous surgery and presented this time with persistent symptoms or worsening symptoms which required revision surgery.

Procedure done

The majority of the patient had either single Lobectomy (54.5%),bilobectomy(16%) or pneumonectomy (23%). In a small number of patients segmentectomy was done (6 patients). Lobectomy along with segmentecomy was done in 10 patients.

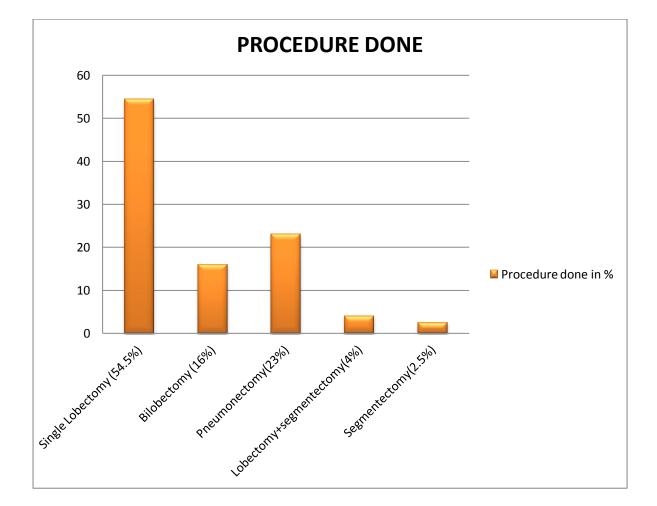


Figure-13

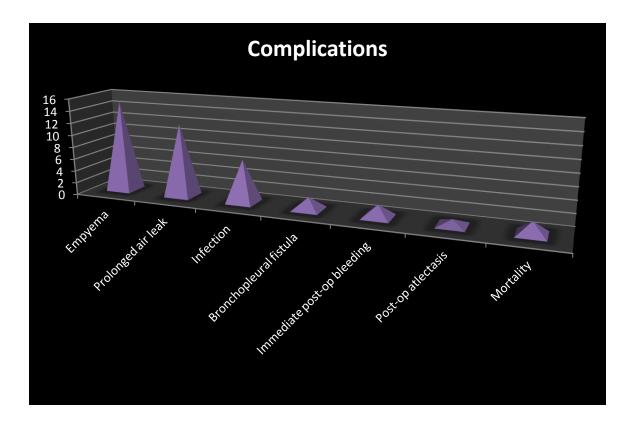
Complications

There were 39 patients who had complications which accounts for 16% of the total patients in our series.

Out of these patients 15 of them had empyema post-operatively, 12 patients had prolonged air leak, 2 patients had Bronchopleural fistula, 2 patients had immediate post operative bleeding, and 1 patient had atelectasis. There were 2 mortality.

Table-2

S.No	complication	No of patients
1.	Empyema	15
2.	Prolonged air leak	12
3.	Infection	7
4.	Bronchopleural fistula	2
5.	Immediate post-op bleeding	2
6.	Post-op atlectasis	1
7.	Mortality	2



The post-operative management of the complications were one of the following like Re-thoracotomy for bleeding, BPF closure, Intercostal drainage and window procedure .

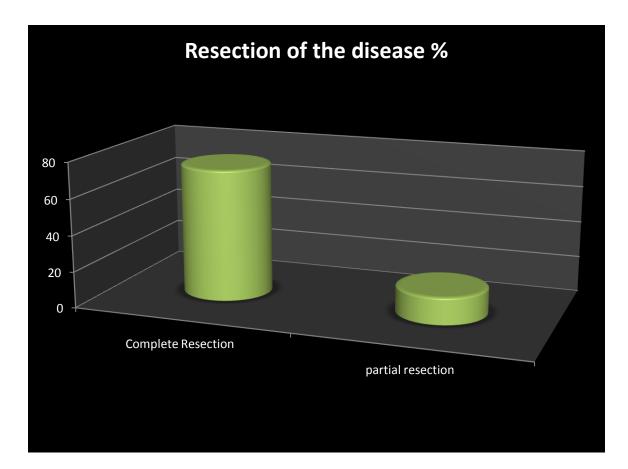
Table-3

S.No	Complications	No of patients
1.	BPF closure	2
2.	ICD insertion	12
3.	Re –thoracotomy	2
4.	Window procedure	7

Post op analysis

Complete resection of diseased portions of the lung was achieved in in 85% of the people and 15% of the had residual disease elsewhere.

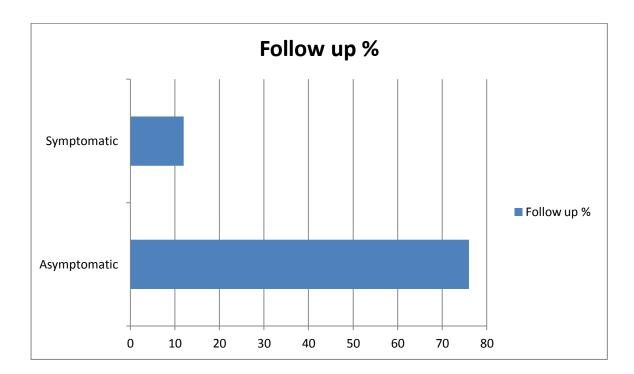




Follow up

In the follow up period after surgery 76% were completely asymptomatic, 12% had residual minor symptoms. 12% of our patient did not have a proper follow up.

The average follow up of our patients is 5.1 years (range from 1 month to 13 years)



Analysis of symptomatic and asymptomatic patients post-operatively

The variables were calculated using chi-square test.

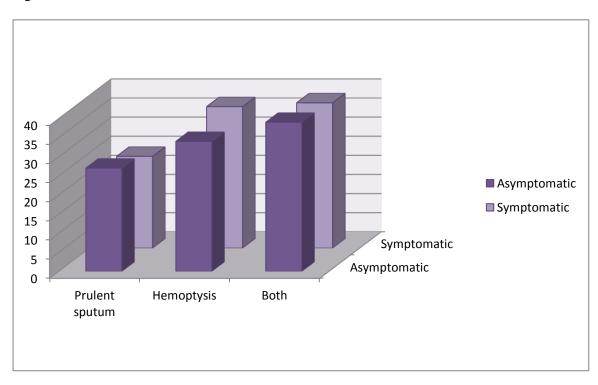
The p-value <0.05 indicates a significant association between outcome and other variables

Table-4

		Asymptomatic		Symptomatic		
variables	group	n	%	n	%	p-val
symptom	purulent sputum	36	26.67	7	24.14	
	haemoptysis	46	34.07	11	37.93	
	both	53	39.26	11	37.93	0.92

It is observed from our study that the mode of presentation like purulent sputum or haemoptysis has no statistically significant association p value is >0.05





Association between procedure done and outcome

The various procedures done for the treatment and the outcome after surgery appears not associated in our study as the p value is 0.97

Table-5

		asymptomatic		symptomatic		
variables	group	n	%	n	%	p-val
procedure						
	Lobectomy	94	71.76	21	72.41	
	Pneumonectomy	29	22.14	6	20.69	
	Segmentectomy+segmentecto					
	my with lobectomy	8	6.11	2	6.90	0.97

The following bar diagram depicts the procedure done to outcome of the patient

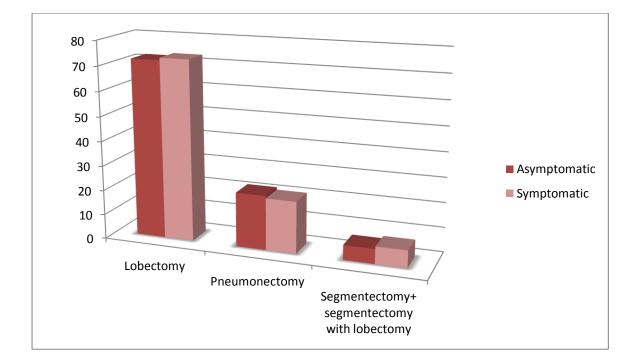


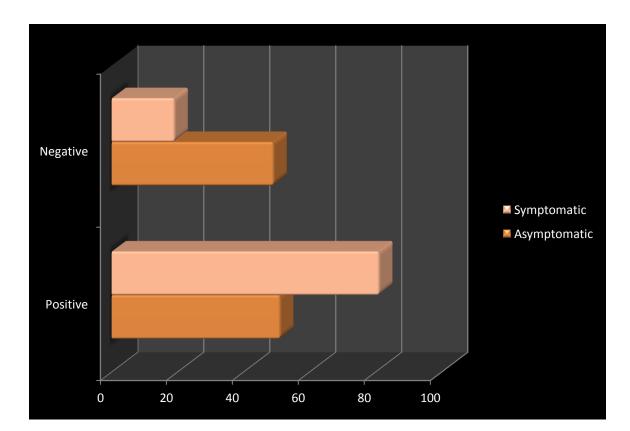
Figure-18

Association between sputum culture positivity and post operative symptoms

Table-6

		asymptomatic		symptomatic		
variables	group	n	%	n	%	p-val
sputum						
culture	positive	51	51	13	81.25	
	Negative	49	49	3	18.75	0.024

It is observed that patients with significant bacterial infection as per cultures pre operatively, continued to have some symptoms post operatively also even after successful resection. (p value 0.024). It is shown in the following diagram



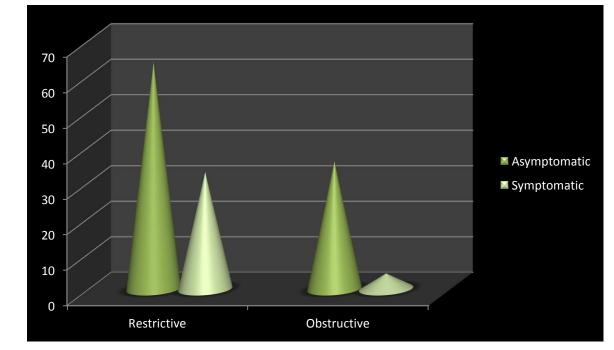
Association between PFT and outcome

In patients with evidence of obstructive disease in PFT were more often symptomatic even after surgery (p value 0.005). Thus there is a strong association between the preoperative state of the lung or the pulmonary reserve and the outcome after surgery.

Table-7

		asymptomatic		symptomatic		
variables	group	n	%	n	%	p-val
PFT	Restrictive	76	64.41	8	33.33	
	Obstructive	42	35.59	16	66.67	0.005

The association between the PFT and the outcome is shown in the following figure



Association between completeness of resection and outcome

Patients in who complete resection was possible had no post operative symptoms as opposed to those who had residual disease after resection who remained partially symptomatic. This association was statistically significant.

Table-8

		asymptomatic		symp		
variables	group	n	%	n	%	p-val
	Complete					
Follow up	eradication	50	100	4	14.29	
	Incomplete					
	eradication	0	0	24	85.71	<0.001

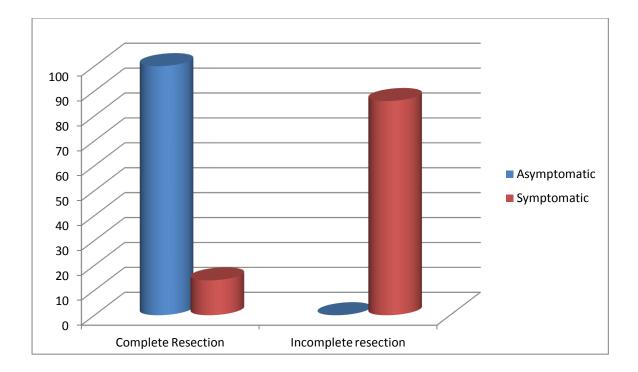


Figure-21

The above figure shows the significant association between the resection of the disease and outcome.

Association between outcome and residual Bronchiectasis

Table-9

		asymptomatic		symptomatic		
variables	group	n	%	n	%	p-val
Residual						
Bronchiectasis	No	135	100	2	6.9	
	Yes	0	0	27	93.1	< 0.001

It is evident from the above table that presence of residual disease is single most important factor which accounts for 93% of symptomatic patients. From the p value <0.001 it is clearly proved that this variable is strongly associated with the outcome.

The following diagram shows the association between the variable and outcome.

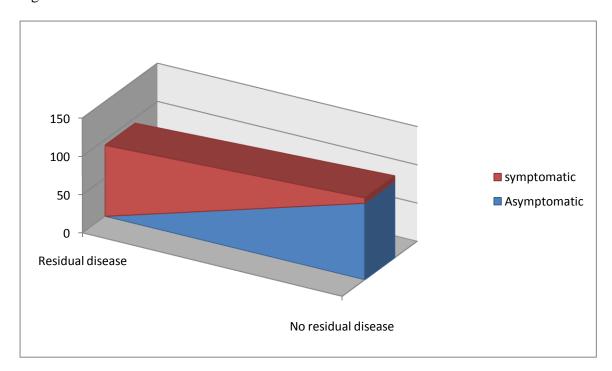


Figure-22

Discussion

Bronchiectasis is a chronic condition characterised by abnormal dilatation of the affected bronchi. Before the antibiotic era it was a dreadful disease resulting in significant number of patients landing in respiratory failure and cor pulmonale. The exact prevalence of the disease was difficult to ascertain.

We analysed 242 patients retrospectively who underwent surgical treatment for Bronchiectasis between 1992 - 2012. All the patients who were operated upon were included in the study and those patients who were not fit for surgery of those who refused surgery were excluded from the study.

Out of the 242 patients analysed, majority of them were males (64%) while the remaining 36% were females (figure-1). This increased incidence in males is noted in most of the other series like Balkanli et al, cayalak et al. However, kutlay et al found higher incidence in females(55%). This higher incidence among men may be due to the higher prevelance of smoking and substance abuse among men in our country, The availability of over the counter drugs for cough and expectoration and delay in seeking medical attention are also factors that are responsible for the increased incidence in males who are the bread winners of the family and thus do not have the time or money to spend on doctors..

In our series the minimum age of the patient who underwent surgery is 12 years old, with maximum we operated on a 66 year old patient(figure-2). The median age is 34 years(table-1). It is observed that majority of our patients were between the age group 20-40(figure-2). The median age of the patient was same as observed in kutlay et al

In our study group majority of the patients presented with Haemoptysis (45%). Chronic cough with expectoration was present in 40% of our patients. However 14% of the patients had both Haemoptysis and expectoration.

Reda Alfaei et al, Kutlay et al, found that recurrent infections with expectoration of copious foul smelling sputum was the common presenting symptom. In India, haemoptysis, being a more alarming symptom makes the patient seek medical attention rather than the copious expectoration which is often a neglected symptom for reasons mentioned earlier.

Duration of symptoms before surgery had a wide range from as less as to 1 month to as long as 34 years in a patient. The average duration of our patients is 5.5 years. In Kutlay et al the mean age is 5.7 years which is similar to our study. This long duration of the symptoms is primarily due to long indolent nature of the disease. Only the presence of a streak of haemoptysis, makes the patient opt for surgery.

The improvement in the standard of medical care including availability of inhaled macrolides, use of steroids etc has delayed or decreased the number of patients requiring surgery.

Like other studies majority of our patients (56%) had disease involving the left side only, 33% had disease on the right side only on right and 11% had bilateral disease.

Gravity makes the purulent secretions pool in the the lower lobes, making them more prone for the development of Bronchiectasis. The incidence is higher on the left side as compared to the right since the left main bronchus is a more acute angle to the midline than the right. Thus the mucociliary clearance is better in the right lung. The left main bronchus is narrower and longer than the right making it more vulnerable to blockage, due to enlarged peribronchial lymph nodes or viscid sputum. However, foreign body aspirations are more common on the right side

In a study by Caylak et al, 66% of the patients had left sided disease which is more than our series. However in most studies like in the series by Kutlay et al, King PT et al, the side incidence is similar to that in our study.

Middle lobe is more frequently affected because of its long and slender with acute normal angulations, prone to being compressed by enlarged lymph nodes.

About two thirds of our patients (73%) was taking antibiotics regularly as prolonged short courses (>14 days) or long term antibiotics (> 6 weeks) to control repeated chest infection. Along with antibiotics about 63% of the patients were on bronchodilators. In our series 58 % of them had taken Anti-Tuberculous medicines. The incidence of ATT is slightly higher when compared to western studies probably because of the higher prevalence of Tuberculosis in our community and the arbitrary usage of these medications without proper confirmation of tuberculosis. Average duration of medical therapy before surgery is 4 years which is similar to the study done by Kutlay et al. Maximum duration of medical therapy in our series is 15 years.

With regards to investigations, plain chest X-ray alone was diagnostic of Bronchiectasis in 64%. This incidence is higher when compared to other studies like Balkalni et al, Kutlay et al. The reason for this increased sensitivity of X-ray may be the delayed presentation of the patients where the features are obvious for diagnosing even in

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x-ray. In western literature, perhaps due to early presentations, the chest X-ray is less sensitive.

About 16% of our patients had typical features like multiple cysts with air fluid levels suggestive of Bronchiectasis. Such a picture in chest X-ray will appear only late in the course of the disease. In our study group about 15% had features like consolidation in chest X-ray. Localized Bronchiectasis confined to single lobe may appear as mass lesion in X-ray a finding in about 5% of our patient. However, the reliability of the chest x-ray as a diagnostic tool is not good and a HRCT is mandatory for accurate diagnosis especially before subjecting any patient for surgery.

Thus an high resolution computed tomography (HRCT) is the imaging modality of choice for investigating a case of Bronchiectasis. In our series 93% of the people had features suggestive of Bronchiectasis without much diagnostic dilemma. In addition to the diagnosis of bronchiectasis, it can pick up other co-existing pathology. A completely destroyed lung was seen in 11% of the patients, concomitant pleural effusion in 2%, and co-existing neoplasm was diagnosed in less than 1 % (3 patients).

Pulmonary function testing (PFT) was carried out in all the patient undergoing surgery. It showed obstructive pathology in 56% and restrictive pathology in 44%. The higher number of patients with obstructive pathology may be due to co- existent COPD. More patients with obstructive pathology in PFT had residual symptoms post operatively than those with restrictive pathology in PFT pre operatively. This finding was statistically significant (p value 0.005). Hence the pulmonary reserve of the individual as well as the baseline PFT has significant impact on the outcome.

All the patients had sputum cultures done. In our study group we found that 57% of the people showed positive sputum cultures whereas only 43% showed no growth. This is on par with other studies like King PT et al where the sputum positivity was 62%. In those who have sputum positivity, a mixed growth of organisms were isolated in 50% (figure-10) and specific organisms were isolated in the remaining 50%. Among the organisms isolated in our group, H.influenzae accounted for 26%, followed by Pseudomonas in 18% and Strep. pneumonia 6%. Other studies like Angrill et al has shown Pseudomonas as the principle respiratory isolate in their series. In patients with immunocompromised state also, the primary isolate was pseudomonas. In Kutlay et al like our study the most common organism isolated was H.influenzae. Presence of pre operative infection in the sputum had an direct correlation to the persistence of symptoms post operatively (p value 0.024) Bronchoscopy was done in all patients undergoing surgery. The primary aim of bronchoscopy was to rule out any foreign body associated with the Bronchiectasis, associated bronchialstenosis or intra luminal or extrinsic compression. We had 12 patients (0.05%) who had significant findings in the bronchoscopy (figure-11). A bronchoalveolar lavage was also useful in initating the appropriate antibiotic.

The main indication for surgery in our group is a history of repeated cough with expectoration (48%) followed by haemoptysis accounting for 48% of the patients operated.

The common indication in other studies were repeated infections as per Bagerhi et al (77.1%) and Reda alfaie et al (71.7%). When compared to these studies this indication for surgery in our series is less.

Haemoptysis is the other significant indication in our study (48%) which, when compared to Reda alfaie et al (15.9%) is almost triple the number. (figure-12).

The commonest surgery done in our study is single lobectomy (54.5%), followed by pneumonectomy (23%). Zhang p et al while analysing a group of 790 patients found lobectomy(72%) to the commonest. In Bagheri et al the lobectomy was done only in 42%, less than in our series. Its obvious that that lobectomy is the procedure of choice when the disease is confined of localised to a lobe. More aggressive removal of lobe when it is not macroscopically diseased is not advised in the literature. For disease involving more than two lobes with CT evidence of disease in the third lobe , pneumonectomy may be considered in order to prevent relapse of symptoms earlier. When the disease was localised to a small segment or lingula alone then a segmentectomy or a lingulectomy is warranted.

39 patients (16%) who underwent surgery had post operative complications. Commonest complication in our series was post operative empyema in 15 patients(0.06%), prolonged air leak in 12 patients (0.05%), post operative infection in 7 patients, bronchopleural fistula in 2 patients, atelectasis in 1 patient and immediate post-operative bleeding in 2 which required re-thoracotomy for controlling it.

When compared to Hiramatsu et al (18%), the overall complication rate in our group(16%) is slightly less. The complication rate (16%) is on par with Bagheri et al (15.8%). The infection rate in our series (2.8%) is less when compared to Bagheri et al (5.7%). There mortality in our series is 0.8%(2 patients) which is comparable to other series like Bagheri et al and Zhang p et al. The post-operative complication management included BPF closure in 2 patients, window procedure in 7 patients and re-exploration for bleeding in 2 patients.

In our series, complete resection of the macroscopic disease was done in 85% of patients. In 15% of the patients there was residual disease elsewhere in the lung .Partial resection of the disease included bilateral disease in which unilateral lobectomy done, minimal disease in the other lobes as evidenced by CT but macroscopically healthy looking lobes. When compared to Reda Alfaie et al (94%) the complete resection rates in our series is low. The incomplete resection group had a statistically significant symptoms after surgery (p value <0.001).

The outcome of our study is based on whether patient is free of symptom or is the patient symptomatic after the surgery. Univariate analysis of this variable was done using chi square test, a p value of less than 0.05 is considered significant association.

It is statistically proven that the presenting symptoms like purulent sputum, haemoptysis is not associated with the outcome (, p value 0.92). Similarly in our series the procedure done whether it is lobectomy, pneumonectomy or segmentectomy did not show statistical significance with regards to post operative symptoms (p value 0.97).

However the presence of a positive culture pre operatively was associated with persistence of post operative symptoms. (p value 0.024). In the patient with persistence symptoms post operatively, 81% of the people had sputum positivity.

An obstructive PFT affected the post operative symptoms (p value0.005). 67% of the patients who were symptomatic post operatively had obstructive pathology in PFT pre operatively.

The extent of surgical resection whether complete or incomplete has a strong statistical significance to the outcome, p value being <0.001. It is noted that 86% of the patients who were symptomatic after surgery had residual minor disease elsewhere in lung. . In our group 93% of the patients who were symptomatic after surgery had had residual Bronchiectasis.

76% of our patients, as comparable to Dogan et al (80%) were totally asymptomatic after resection. Compared to Bagheri et al (58%) the patients in our series has a better symptomfree life after surgery.

Sequential resection for bilateral disease could be planned about 6 weeks apart. Two of our patients had had thoracotomy and resection on the opposite side for removal of a diseased segment.

Conclusion

Bronchiectasis is primarily a medical disease which requires careful assessment and diagnosis. Once diagnosis is made, the patient should be under medical surveillance and treatment for repeated infections and haemoptysis. Appropriate antibiotics as dictated by cultures should be initiated in order to avoid progression of the disease. If and when surgery is indicated, a thorough pre-operative evaluation should be carried out. As in other literature, our study also proves that surgical treatment for Bronchiectasis can be done safely with minimal acceptable mortality and morbidity. Single most important factor which decides on the symptom free state after surgery is the adequacy of the resection. Complete resection of the localised Bronchiectasis offers better cure as well as symptom free survival after surgery. However it should be appreciated that in cases of diffuse bilateral disease, post operative residual Bronchiectasis is unavoidable. In such cases, though the intensity of symptoms may improve greatly after surgery, minimal symptoms may persist.

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APPENDIX I

MASTER CHART