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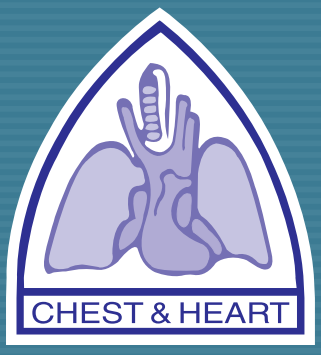

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EDITORIAL

Management of post-COVID-19 lung fibrosis: It's the high time for the Pulmonologists to show their wisdom

[Chest Heart J. 2020; 44(2) : 57-60]
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It's nearly one and a half year have passed since the world first encountered one of the deadliest tsunami of this century – the coronavirus disease (COVID-19). At the time of writing this editorial, globally there are 177,435,887 cases, which cost 3,842,319 lives. Bangladesh is also not out of this inferno. Currently we are facing the second wave with a burden of 8,41,087 cases and 13,345 deaths.[1]

Viral infection has a potential to cause airway epithelial injury, apoptosis, and long standing lung damage.[2] The mechanism of post-viral lung fibrosis has been extensively studied in other influenza epidemics. Looking back at severe H1N1, a study in China among hospitalized patients with pneumonia caused by the 2009 H1N1 influenza showed high levels of transforming growth factor beta 1 (TGF β1).[3] In the SARS CoV 1 outbreak in 2002, high levels of TGF β1 were also observed in serum and bronchoalveolar lavage.[4]This cytokine is known to induce fibrosis by various mechanisms which include increased deposition of extracellular matrix proteins, stimulation of fibroblast chemotactic migration, and fibroblast to myofibroblast transition. In the current SARS CoV 2 pandemic, the molecular basis of progression to pulmonary fibrosis is still unclear but is believed to be multifactorial. Direct viral effects, the upregulating effect of the virus on cytokines like TGF β1, IL-6, IL-1 and, increased oxidative stress have all been postulated.[5] There is a pivotal role of the renin–angiotensin system, as the high affinity binding between the SARS CoV 2 viral spike protein and the angiotensin converting enzyme 2 (ACE 2) receptor has been shown to downregulate the level of the ACE2 receptor.[6] The decreased ACE 2 expression, in turn, leads to high angiotensin-2 levels, leading to fibrotic process, signaling cellular and molecular events, and ultimately development of pulmonary fibrosis. The iatrogenic factors potentially contributing to the fibrosis encountered in survivors of severe COVID 19 pneumonia are oxygen toxicity and ventilator induced lung injury (VILI). Patients who develop post COVID fibrosis are invariably those who had extensive, bilateral involvement at the outset, had required high concentrations of oxygen, often for prolonged duration. Extended exposure to high concentrations of oxygen produces oxygen derived free radicals which can damage the pulmonary epithelium.[7]

As we have already known, though most of the SARS-CoV-2 infections are mild to moderate, nearly 5–10% patients may progress to severe or critical disease, including pneumonia and acute respiratory failure.[8,9] Fibrotic abnormalities of the lung have been detected as early as 3 weeks after the onset of symptoms regardless of whether the acute illness was mild, moderate, or severe.[10,11] Abnormal lung function (i.e., restrictive abnormalities, reduced diffusion capacity, and small airways obstruction) has also been identified at the time of discharge from hospital and 2 weeks thereafter.[12] These lung function abnormalities appear to be more common among patients whose acute COVID-19 was severe with high levels of inflammatory markers, and are often accompanied by evidence of pulmonary fibrosis including interstitial thickening, coarse reticular patterns, and parenchymal bands.[13]

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Reviewing literature on other influenza pneumonias, it is observed that H1N1 was only occasionally complicated by fibrosis,[14] whereas as many as 22% of patients with H7N9 pneumonia[15] were left with fibrosis at 6 months. There is limited data from other coronavirus infections such as SARS and Middle East respiratory syndrome (MERS). A study by Chang *et al*.[16] in patients with SARS showed that in follow-up CT scan at 4-6 months, there was significant regression of CT abnormalities. The only long term longitudinal data on MERS by Zhang *et al*., which followed up 81 health care workers with MERS for a period of 15 years.[17] They found that only 5% of patients had residual interstitial fibrosis at 15 years. Variable outcomes have been noted in several studies on COVID-19 patients. A follow up study by Zhao *et al*.[18] of pulmonary function and radiology in 55 COVID 19 survivors 3 months after recovery showed that 71% had residual CT abnormalities, including evidence of interstitial thickening in 27%. A prospective, multicenter, observational study on 86 severe COVID-19 survivors in Austria[19] found that the majority of patients were left with persisting dyspnea (37%), reduction in diffusion capacity (28%), and CT abnormalities (88%) at 6 week post-discharge. At 12th week, there was remarkable improvement of CT abnormalities. Follow up of cohorts of post COVID survivors are already underway at several centers in different countries. The burning question is: whether the chest CT scan abnormalities likely to persist, gradually improve, or even worsen with the passage of time? Long-term follow-up of these patients is the only answer of this question. So, which follow-up model we can apply? Raghu *et al*.[20] have proposed a follow up scheme for these post COVID survivors. They argued for an initial baseline visit once the patient is polymerase chain reaction negative with a baseline non-contrast HRCT, PFTs (spirometry, lung volumes, and diffusion capacity), 6 min walk test, and assessment of quality of life (QOL) with standard questionnaires. Thereafter, to better understand the natural course of the disease, they suggest follow up visits, either remotely or in person at frequent interval up to a total duration of 36 months, based on the degree and extent of lung involvement. Applying this model is not feasible in a resource-limited country like us. We may propose a visit at 3, 6, 9, and 12 month, with lung function test, QOL assessment in each visit and HRCT at 6th and 12th month.

Lot of debate and controversies have been arisen regarding the management of post-COVID lung injury. The role of antifibrotic drugs in the prevention and treatment of post COVID fibrosis is unclear at present. Both COVID and IPF share many common demographic factors, disproportionately affecting males, the elderly, and smokers. These drugs are also believed to be useful in patients with acute exacerbations of ILD (both IPF and other fibrotic ILDs). Finally, fibrosis with fibroblasts and honeycombing has clearly been demonstrated in autopsies of COVID-19 patients. For all these reasons, it is reasonable to assume that antifibrotics may have a potentially valuable role in this setting.[2] Pirfenidone and nintedanib are antifibrotic drugs that, despite having differing modes of action, are similarly effective in attenuating the rate of lung function decline by about 50%.[21,22] Pirfenidone is a pyridone with a poorly understood mechanism of action and nintedanib is a tyrosine kinase inhibitor. These two agents, established to be useful in IPF and other progressive fibrotic ILDs, are known to inhibit experimental lung injury and inhibit IL 6, IL 1, and IL 1B. It is worth noting that both these drugs take at least 1–3 months to demonstrate an effect. This is the time period at which the FVC starts to improve compared to placebo as shown in the INBUILD, INPULSIS, and ASCEND trials.[21-23] CT scan evidence of fibrosis with traction bronchiectasis and/or honeycombing would be useful to identify which patients would potentially benefit from antifibrotics. Though the role of steroid is well proven to treat hypoxaemic COVID patients in RECOVERY trial,[24] steroids alone may not be sufficient to prevent the development of fibrosis.[2]

The benefit of antifibrotic medication in COVID-induced lung injury is still putative. Trials are ongoing in different centers, and we have to wait some more days to come to a conclusion. It is disappointing to observe that some physicians are prescribing these drugs without knowing a clear indication, in a wrong dosage and duration. This malpractice must be eschewed, as these drugs are costly, have side-effects, and will cast a burden over the patients. It is strongly recommended that

antifibrotics should be reserved for those post COVID patients who demonstrate definite evidence of disease progression. Prescribing these drugs to those who are spontaneously improving over time or whose fibrosis is static, is a criminal offence.

The Chest and Heart Association of Bangladesh and Bangladesh Association for Bronchology and Interventional Pulmonology (BABIP) have mounted a task-force to formulate a precise guideline for the appropriate management of post-COVID pulmonary sequelae.

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ORIGINAL ARTICLE

Cytomorphological Pattern, Evaluation of Serum Adenosine Deaminase (ADA) Level and Clinical Presentation of Peripheral Lymph Node Tuberculosis – An Observational Study

Nirmal Kanti Sarkar[1], Md. Ashadur Rahman[2], Moumita Roy[3], Jesmin Akter[4], Mohammad Mosharaf Hossain[5], Md. Serazul Islam[6], Abdullah Al. Mujahid[7]

Abstract:

Background: *Lymphadenitis is the most common form of extrapulmonary TB. Fine needle aspiration cytology (FNAC) is the most commonly used diagnostic tool. This study observed the cytomorphological pattern, serum adenosine deaminase (ADA) level and clinical presentation of lymph node TB.*

Methods: *We conducted a cross-section, observational study at the 250-Bedded T.B Hospital, Shyamoli, Dhaka, Bangladesh between January 2019 -January 2020 among the patients with peripheral lymphadenopathy and compatible clinical features favoring tuberculous etiology attending at the outpatient and inpatient department. Patients were categorized in three groups according to the lymph node FNAC pattern. Clinical presentation and radiological findings were evaluated and serum ADA level was estimated. Any association between lymph node cytology and serum ADA level was sought.*

Results: *Total 36 patients were enrolled in the study. Among them 75% were female and the mean age was 33.5±14.6 years. All the patients had cervical lymphadenopathy, and 83.3% had matted lymph nodes. Eighty six percent patients had high serum ADA level above cut-off value. The most common cytomorphological pattern observed in lymph node FNAC was epithelioid granuloma with caseous necrosis (58.3%). There was significant relationship between lymph node cytomorphological pattern and serum ADA level ($p<0.05$).*

Conclusions: *Tuberculous lymphadenitis is more common among female than male. Most common site of lymph node TB is cervical region, and epithelioid granuloma with caseous necrosis is the most frequently observed cytological pattern. Serum ADA is shown to have a potential role to support the diagnosis of tuberculous lymphadenitis.*

Key words: *Adenosine deaminase (ADA), cytomorphology, fine needle aspiration cytology (FNAC), lymph node tuberculosis (LNTB)*

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Introduction:

Tuberculosis remains a major health burden and is one of the top 10 causes of death worldwide. In 2018, an estimated 10.0 million people were infected with TB, and there were 1.2 million TB deaths among HIV-negative people. It has been the leading

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cause of death from a single infectious disease. Bangladesh ranks 7th among the top ten leading countries of global TB burden, with an incidence rate 221/100 000 population.[1]

The main form of the disease is highly transmissible pulmonary TB. Extrapulmonary TB (EPTB) is the infection of sites other than the lungs.[2] Lymph nodes are the most common site of EPTB and accounts for upto 40% of extrapulmonary disease in the USA.[3] A country wise data is not available.

Different studies reported that the peak incidence of lymph node TB (LNTB) is in young adults between 20 and 40 years.[4-6] Female sex, ethnic variety, and poor immune status is associated with the development of LNTB.[7,8] The disease is particularly common in persons with HIV co-infection.[9] Most LNTB involves cervical region and presents with a painless, erythematous, firm mass commonly involving anterior and posterior cervical chain or supraclavicular LN.[10] Progression of the disease is associated with fluctuation and sinus formation.[4, 7]

The diagnosis of LNTB involves fine needle aspiration cytology (FNAC), or excisional biopsy with histopathology, examination of acid-fast bacilli (AFB), and mycobacterial culture or PCR of lymph node aspirates.[10] Epithelioid granuloma with or without caseous necrosis is the prototyped cytological finding. AFB smear is positive in only 25-50% cases and culture in 70-80% cases.[11] Chest X-ray should be done in all patients with suspected TB to evaluate associated pulmonary TB or involvement of mediastinal lymph nodes. Adenosine deaminase (ADA), an enzyme of purine catabolism, is present in an increased concentration within lymphocytes. It has been shown that T lymphocyte population is increased in TB, and hence the activity of ADA is also increased.[12] Measurement of adenosine deaminase activity is very simple. It can be estimated by commercial ADA-MTB kit. The principal is ADA hydrolyses adenosine to ammonia and inosine. The ammonia which is formed further reacts with phenol and hypochlorite in an alkaline medium to form blue indophenol complex with sodium nitroprusside acting as a catalyst. Intensity of blue colored indophenol complex formed is proportional to the amount of ADA present in the sample.[12] The validity of serum ADA in the diagnosis of tuberculous pleural and pericardial effusion and tuberculous meningitis is established.[13, 14] But there is paucity of data regarding its role in the diagnosis of LNTB.

This study examined the cytomorphological pattern of LNTB in FNAC, depicted the clinical presentation, and estimated the serum ADA concentration as a supporting biomarker in the diagnosis of tuberculous lymphadenopathy.

Methods

We conducted a cross-section, observational study at the 250-Bedded T.B Hospital, Shyamoli, Dhaka, Bangladesh, a government referral hospital for the management of tuberculosis patients, over a period from January 2019 to April 2021. Data collection was temporarily aborted from March 2020 to August 2020 due to CoVID-19 situation. Thirty nine patients with peripheral lymphadenopathy and compatible clinical features favoring tuberculous etiology attending at the outpatient and inpatient department of the hospital were preliminarily enrolled in the study. Three patients were discarded, as fine needle aspiration cytology (FNAC) result revealed non-specific lymphadenitis. Thirty six patients with FNAC diagnosis compatible with tuberculous etiology were included in the final analysis. Detailed history, thorough physical examination, relevant hematological investigations, Mantoux test (MT), chest X-Ray, and serum adenosine deaminase (ADA) estimation were carried out. All cases were categorized cytologically into three groups as suggested by Das et al.[15] The cytomorphological patterns were: epithelioid granuloma without caseous necrosis (pattern A), epithelioid granuloma with caseous necrosis (pattern B), and caseous necrosis without epithelioid granuloma with neutrophilic infiltrate (pattern C). A skin induration more than 10 mm in Mantoux test and the serum ADA more than 15 U/L were considered as significant. Statistical analysis was conducted using SPSS v23.0 (IBM Corp. Armonk, NY, USA). Data were presented in both univariate and multivariate tables according to merit. Chi-square test was done to correlate cytomorphological pattern of lymph node FNAC and serum ADA. A 'p value' <0.05 was considered as significant.

Results:

The study included 36 patients in total. The demographics and clinical features are summarized in Table I and Table II accordingly. The mean age was 33.5±14.6 years with a range between 15 to 68 years. Lymph node TB had a higher proportion among female (75%) compared to male (25%). Only a few patients (5.6%) had a previous history of TB. More than 90% patients had symptoms persisted for more than four weeks. All the patients had neck swelling, and 5 patients had enlarged lymph node in other locations in addition. Majority of the patients had right cervical adenopathy (55.6%), and 11.1% had bilateral involvement. In most of the cases lymph nodes were matted (83.3%) (Table III). Fever (86.1%), weight loss (66.7%), and dry cough (41.7%) were the other most common presenting features in chronological order. More than eighty percent patients had normal chest X-ray, and 11% had mediastinal lymphadenopathy (Table IV). Twenty five patients (63.9%) had a skin induration more than 10 mm in Mantoux test (Table V). Eighty six percent patients had high serum ADA level above cut-off value (15 U/L), ranging between 6.65-58.5 U/L (Table VI). The most common cytomorphological pattern observed in lymph node FNAC was pattern B, i.e. epithelioid granuloma with caseous necrosis (21 patients, 58.3%) followed by pattern A, i.e. epithelioid granuloma without caseous necrosis (14 patients, 38.9%) (Table VII). Significant association was observed when lymph node cytomorphology pattern was compared with serum ADA level (p value 0.034) (Table VIII).

Table-I

Demographic characteristics

Variables	Frequency	Percentage
Age (years)		
≤20	9	25.0
21-30	12	33.3
31-40	3	8.3
41-50	6	16.7
51-60	5	13.9
>60	1	2.8
Mean±SD	33.5	±14.6
Range (min-max)	15.0	-68.0
Sex		
Male	9	25.0
Female	27	75.0
Previous H/O TB		
Yes	2	5.6
No	34	94.4

Table-II

Clinical presentation of tuberculous lymphadenitis

Variables	Frequency	Percentage
Duration of symptoms		
<2 weeks	1	2.8
2-4 weeks	2	5.6
>4 weeks	33	91.7
Clinical presentation		
Neck swelling	36	100.0
Fever	31	86.1
Weight loss	24	66.7
Dry cough	15	41.7
Chest pain	5	13.9
Swelling at groin/axillae	4	11.1
Sputum production	4	11.1
Haemoptysis	2	5.6

Table-III

Lymph node characteristics

Lymph node	Frequency	Percentage
Site		
Cervical		
Right	20	55.6
Left	12	33.3
Both	4	11.1
Cervical and Axillary	4	11.1
Cervical and submental	1	2.77
Character of LN		
Matted	30	83.3
Discrete	3	8.3
Cold abscess	3	8.3

Table-IV

Radiological findings

Radiological findings (Chest X-ray)	Frequency	Percentage
Normal	29	80.6
Mediastinal adenopathy	4	11.1
Consolidation and cavitation	2	5.5
Pleural effusion	2	5.5

Table-V

Pattern of skin induration in Mantoux test

Mantoux test (mm)	Frequency	Percentage
<10	11	30.6
10-20	14	38.9
>20	9	25.0
Not done	2	5.6
Mean±SD	14.1	±7.6
Range (min-max)	0.0	-27.0

Table-VI

Serum adenosine deaminase (ADA) level

Serum ADA (U/L)	Frequency	Percentage
≤15.0	5	13.9
15.1-30.0	19	52.8
>30.0	12	33.3
Mean±SD	26.1	±11.2
Range (min-max)	6.65	-58.5

Table-VII

Cytomorphological pattern of tuberculous lymphadenitis

Cytological pattern	Frequency	Percentage
Epithelioid granuloma without caseous necrosis	14	38.9
Epithelioid granuloma with caseous necrosis	21	58.3
Caseous necrosis without epithelioid granuloma	1	2.8

Table-VIII

Association between lymph node cytomorphology and serum adenosine deaminase (ADA) level in univariate analysis

Cytological pattern	Total No. of cases	Serum ADA		P value
		≤15.0 U/L	>15.0 U/L	
Epithelioid granuloma without caseous necrosis	14	1 (7.1%)	13 (92.9%)	
Epithelioid granuloma with caseous necrosis	21	3 (14.3%)	18 (85.7%)	0.034[s]
Caseous necrosis without epithelioid granuloma	1	1 (100.0%)	0 (0.0%)	

(s= significant, P value reached from chi square test)

Discussion:

This study significantly expanded previous observations that lymph node FNAC is a safe, simple and cost-effective outpatient procedure for the diagnosis of peripheral LNTB.[16,17] We categorized FNAC results into three cytomorphological pattern proposed by Das et al.[15] Pattern A – epithelioid granuloma without caseous necrosis, pattern B – epithelioid granuloma with caseous necrosis, and pattern C – caseous necrosis without epithelioid granuloma with neutrophil infiltration. The most common pattern observed in our study was pattern B (58.3%) followed by pattern A (38.9%). Findings show similarities with other studies.[16, 18-20] The formation of granuloma is dependent on good immune response against the organism. Skin induration in Mantoux test is an indirect evidence of immune response against *M. tuberculosis.*

The female to male ratio was 3:1, which is consistent with previous reports.[2, 3, 7, 8, 21-24] The reason for female predominance is not well understood. It is hypothesized that a difference in tumor necrosis factor (TNF) and IL-10 between both sexes may play a role.[32] Other contributing factors include CD4+ lymphocyte count, endocrine effects, socio-economic and cultural background.[26]

TBLN may occur in any age group. In this study, the peak incidence was seen between 21-30 years and mean incidence 33.5±14.6 years. This finding correlates with other observations.[4-6, 16, 27, 28]

We found that cervical lymph nodes were involved in all patients, and 11% had concomitant axillary lymphadenopathy. Masilamani et al. found 97.2% cervical LN involvement.[10, 29] Similar observations were noted by Chand et al.[30] The organism usually gains access to the cervical LN through the tonsillar LN. More than 80% patients had matted lymph node in our study, which correlates with the studies by Dandapat[31] and Subrahmanyam.[32] Lymph node morphology depends on the stage of presentation. The delayed the presentation, the more complicated the disease. We noted that 91.7% patients presented after 4 weeks of their illness.

Other than lymphadenopathy, fever was the most common clinical presentation (86.11%), followed by loss of body weight (66.7%). Dandapat and Subrahmanyam also found weight loss as the most common feature (85% and 78% accordingly)

followed by fever (40% and 45%).[31,32] Many patients with LNTB present with pyrexia of unknown origin or unexplained weight loss. Thorough physical examination including searching for enlarged lymph node is crucial in TB endemic region to come to a diagnosis.

Raised level of serum ADA was observed in most of the patients (>85%) in this study, with a mean value 26.1±11.2 U/L (cut-off value 15 U/L). The values showed significant correlation (p value 0.034) when compared to the lymph node FNAC results. Bhatta et al.[16] also found raised serum ADA in 64.28% TBLN cases, whereas Ninghot et al.[12] and Mugulkod et al.[32] observed a raised level in 93.3% and 83.3% cases respectively. Serum ADA is an indicator of active cellular immunity. This enzyme causes proliferation and differentiation of T cells and maturation of monocytes to macrophage, hence plays a crucial role in granuloma formation.[33, 34] Raised ADA level with strong clinical suspicion with or without a typical cytological feature may help clinicians to reach a confident diagnosis of LNTB.

Conclusions:

Detection of acid-fast bacilli in representative sample is the gold standard for the diagnosis of tuberculosis. But in extrapulmonary TB, it is not always possible due to paucibacillary nature of the disease. FNAC is a simple, cost-effective, minimally invasive, and relatively safe procedure to diagnose peripheral lymph node tuberculosis. However when cytology report is inconclusive, a supportive biochemical marker may add a great value to the diagnostic yield. This observational study proves the diagnostic potential of serum ADA in peripheral lymph node tuberculosis. Further study with a large sample size and comparison with a control group will improve our understanding of diagnostic efficacy of serum ADA.

Author contributions

N. K Sarkar and Ashadur Rahman designed the study, wrote manuscript, and takes equal credit (co-first author). N.K Sarkar, Ashadur Rahman, Moumita Roy, Jesmin Akter and Mosharaf Hossain gathered data, analyzed data and revised the manuscript. N. K Sarkar takes full vouch for the content of the manuscript.

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ORIGINAL ARTICLE

Pleuroscopy in Undiagnosed Exudative Pleural Effusion, Early Experience in Bangladesh

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Abstract:

Background: *Rigid pleuroscopy is an accurate diagnostic method for undiagnostic exudative pleural effusion which is a burden in our country.*

Methods and Materials*: It was a prospective study done in dept. of Thoracic surgery, Dhaka Medical College Hospital (DMCH), Bangladesh, from 1st July 2018 to 30th June 2019 and total 46 patients with undiagnosed exudative pleural effusion were selected and rigid pleuroscopy performed to obtain biopsy.*

Results: *Rigid pleuroscopy showed diagnostic accuracy of 95.7% with minimal complications (6.4%). As visualization is also a part of this procedure it gives an additional strength in the diagnosis which proved to be 100% accurate.*

Conclusion: *It is an excellent diagnostic tool which is accurate, easy to perform, with least complications and less time consuming, so patient turnover is better which is of great advantage in our country.*

Key words: *Pleuroscopy, Rigid pleuroscopy, Exudative pleural effusion.*

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Introduction:

Pleural effusion is a frequently encountered clinical condition which is caused by tuberculosis, malignancy, parapneumonia, congestive heart failure, pulmonary embolism and many other diseases.[1,2] It affects around 300 subjects per 1,00,000 population per year worldwide.[3] Exudative pleural effusions are usually of infectious origin in youth, while malignancies are common in the aged.[1,4,5]

The accurate diagnosis of pleural effusion is challenging because even after thoracocentesis and/or closed pleural biopsy, 25 40% of pleural effusion remains undiagnosed.[6,7] Pleuroscopy also referred to as medical thoracoscopy is generally described as the evaluation of the pleural space. It

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was introduced by Jacobaeus in 1910 as a diagnostic procedure.[8] A visual inspection of the pleural space, drainage of pleural effusion, and performance of pleural biopsies are the commonly performed procedures during pleuroscopy.[9] Rigid pleuroscopy under local anesthesia had been used successfully for pleural diseases. The instrument is easy to manipulate and covers a wider endoscopic field. So it becomes easy to visualize the site of lesion and take biopsy from accurate location which increases the diagnostic accuracy that is not possible in case of thoracentesis and closed pleural biopsy.[10]

Pleuroscopy is considered a safe procedure with a high diagnostic accuracy. The technique of pleuroscopy is similar to that of chest tube insertion and the procedure is easier to learn than

flexible bronchoscopy if competence in chest tube placement has already been gained.[11] The advantage of it over Video Assisted Thoraoscopic Surgery (VATS) is that it doesn't require general anaesthesia and single lung ventilation. Pleuroscopy is akin to chest tube insertion and can be carried out with a single site of entry using local anaesthesia. It is safe when performed by trained persons and we believe that with rapidly advancing technology, improved methods of anaesthesia and technology, pleuroscopy may replace conventional biopsy methods in the near future.[12,13]

In this study we aim to evaluate the diagnostic accuracy and complications of rigid pleuroscopy.

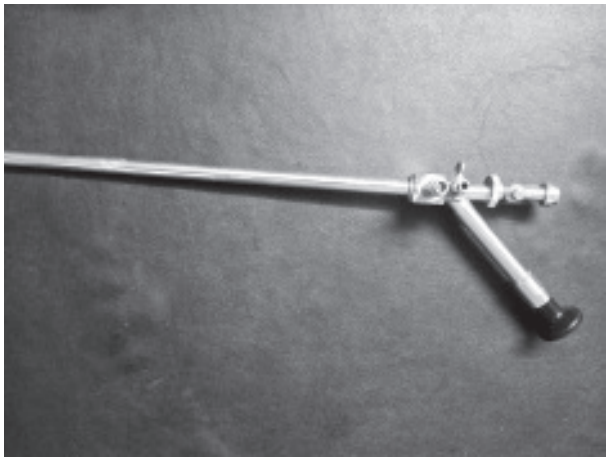

Fig.-1: *Rigid Pleuroscopic Endoscope*

Materials and Methods:

This prospective study was conducted in dept. of Thoracic Surgery, Dhaka Medical College Hospital from 1st July 2018 to 30th June 2019. Total 46 patients with exudative pleural effusion was selected as sample diagnosed by chest x-ray, CT scan of chest and pleural fluid study (Protein, sugar, LDH) in whom diagnosis couldn't be confirmed . Rigid pleuroscopy was done in aseptic technique under local anaesthesia in through 5th or 6th intercostals spaces in mid-axillary line and multiple (5-6) biopsies were taken from parietal pleura in suspicious areas. A 28FR chest drain was placed in the site of pleuroscope introduction. Histopathology was done and patient was followed up to see any complications. A chest X-ray obtained on the next day and drain removed after 48 hours if lung is expanded and the collection is minimal.

Result:

Table-I

Patient Characteristics

Patient Characteristics		% (n=46)
Age	Mean age (years)	47.3 years (Range 20-70 years)
Sex		
	Male	26 (56.5%)
	Female	20 (43.5%)
Side of effusion		
	Right	22 (47.8%)
	Left	22 (47.8%)
	Bilateral	2 (0.4%)
Symptoms		
	Breathlessness	38 (82.7%)
	Fever	16 (34.8%)
	Cough	36 (78.3%)
	Chest pain	15 (32.6%)

Mean age of the patients were 47.3 years, 56.5% male and 43.5% female. Equal number of patients (47.8%) developed right and left sided pleural effusion. 2 patients were bfound to have bilateral disease. Te symptoms they presented with were Breathlessness (82.7%), cough (78.3%), fever (34.8%) and chest pain (32.6%) (Table-1)

Table-II

Pleuroscopic findings

Nodules	28 (60.9%)
Adhesion	12 (26.1%)
Thickened pleura	4 (8.7%)
Normal Pleura	2 (4.3%)

After introducing the pleuroscope visual observation of parietal pleura was done and 60.9% patients showed multiple nodules. Adhesions were present in 26.1% cases, 8.7% revealed thickened pleura and 2 patients had normal pleura (Table–2).

Biopsy was taken from 5-6 suspicious sites in each patient and in Table-3 the results of histopathology have been shown. 95.7% patients were found to have definitive diagnosis. Out of which 60.8% patient had primary and secondary malignancy, but malignant cell in pleural fluid study was found in only 8.7% patients. 26.1% patients were diagnosed as tuberculosis whereas none of them had any evidence of tubercular organism in any cytology or culture. 4.3% patients were diagnosed as empyema thoracis and same percentage of patients revealed normal pleura. In only 2 patients (4.3%) no conclusive results were found.

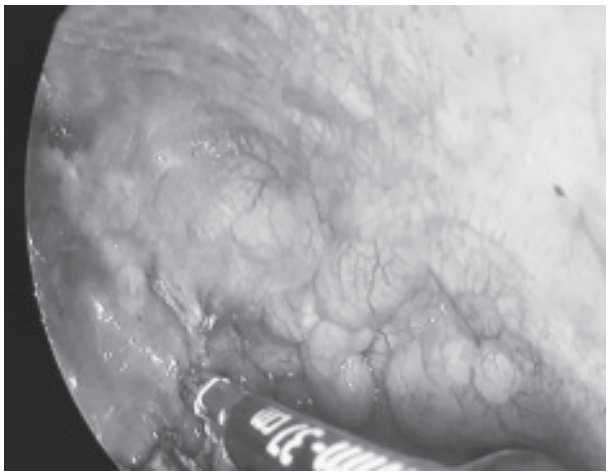

Fig.-2: *Pleural metastasis from Lung adenocarcinoma.*

Table-III

Findings on Histopathology

Findings	%
Metastatic Adenocarcinoma	22 (47.8%)
Poorly Differentiated Metastatic Carcinoma	4 (8.7%)
Mesothelioma	2 (4.3%)
Tubercular Pleuritis	12 (26.1%)
Empyema Thoracis	2 (4.3%)
Thickened Pleura	2 (4.3%)
Normal Pleura	2 (4.3%)

Table-IV

Complications

Subcutaeneous emphysema	2 (4.3%)
Prolonged air leak	1 (2.1%)
Fever	3 (6.5%)
Mild pain	24 (52.2%)

Although Table 4 showing that a large number of patients developed complications it was actually mild pain which was well controlled with NSAIDs. 6.5% patients developed transient fever controlled with paracetamol. Only 2 patients developed surgical emphysema and one patient had prolonged air leak and both were controlled conservatively.

Discussion:

Pleural effusions are a common problem in our Thoracic surgery ward. If a pleural biopsy specimen is needed, a surgeon must usually choose between a blind pleural biopsy and a Pleuroscopic biopsy. In our institute we did pleuroscopy, because most of our patients were referred and they are already on anti TB drugs for more than 3 weeks duration with no clinical improvement and thoracentesis and blind closed pleural biopsy has an diagnostic yield of only 50 60% for combined tuberculosis and malignancy.[7,9,14] In our study 60.8% patients had malignancy whereas only 8.7% were diagnosed to have malignant cell in pleural fluid study. Also 26.1% patients were diagnosed as tuberculosis but none of them had any confirmatory evidence of TB in pleural fluid study. The use of fiberoptic bronchoscopes in the pleural space has been reported previously. Despite providing better views at the apex and paravertebral gutters, it was difficult to control and the diagnostic yield was low.[9] VATS is an excellent alternative with high diagnostic accuracy but needs more expertise and sometime multiple ports. Moreover VATS needs general anaesthesia and related complications are more. In comparison rigid pleuroscopy is done under local anaesthesia and it is technically easy to do.

The primary role for pleuroscopy is to enhance the diagnostic capabilities when less invasive tests fail.[13,15] Rigid instruments have been pivotal in the technique.[16,17] Pleuroscopy with rigid telescopes and trocars provides good visualization of the parietal and visceral pleura. However, with

the single puncture technique, the posterior and mediastinal aspects of the hemithorax are not easily accessed when the procedure is carried out in patients under local anaesthesia. This may necessitate the creation of a second or third port of entry. The presence of adhesions between the lung parenchyma and the chest wall can limit examination, which might account for the false-negative results frequently observed with mesothelioma.[17] This problems can be solved by use of single lung ventilation and collapsing the lung on the site of examination but will require general anaesthesia. So it can be restricted to selected cases where rigid pleuroscopy fails to visualize abnormal pleura. Another alternative is flex-rigid pleuroscopy where areas not visualized in rigid pleuroscopy can be visualized.

In our study diagnostic accuracy of rigid pleuroscopy was 95.7%. This was comparable with most other studies like, Prabhu et al.,[9] Munavvar *et al*.,[18] Wang *et al*.,[19] Blanc *et al*.,[20] Law *et al*.,[21] Tscheikuna,[22] Diacon *et al*.,[23] and McLean *et al*.[24] An excellent evidence of diagnostic accuracy has been shown in our study. Total 28 patients were found to have nodules in parietal pleura when visualized by pleuroscopy and 28 patients were found to have malignancy that is 100%. So it allows the visualization of abnormal areas and a direct biopsy.

In addition to visualization of pleural cavity and to take a biopsy of an abnormal area, it allows for the complete removal of pleural fluid without any additional complication like re expansion pulmonary edema which are more common following closed thoracocentesis when more than 1.5 L of pleural fluid was removed in single sitting. The re expansion pulmonary edema does not occur following pleuroscopy because during the removal of pleural fluid, some amount of air enters through the trocar.[9]

The complications of pleuroscopy are minimal. Only 6.4% developed countable complications (4.3% subcutaeneous emphysema and 2.1% prolonged air leak). This was comparable to Prabhu et al.,[9] Munavvar *et al*.,[18] and Law *et al*.[21]

Conclusion:

So, in conclusion we can say that pleuroscopy is a very much valuable tool in the diagnosis of undiagnosed exudative pleural effusion where thoracentesis failed to yield an accurate diagnosis. It is a simple and safe method that can be done under local anaesthesia with high diagnostic accuracy and with low complication rates. Also this procedure is less time consuming as we have used local anaesthesia and also patient turnover is better which is the best thing in a country like us where patient burden is an important factor to be considered.

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ORIGINAL ARTICLE

Comparative Study of CURB-65, Expanded CURB-65, PSI and SMART-COP Scoring in the Severity Assessment of Community Acquired Pneumonia

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Abstract:

Background and objective: *Community Acquired Pneumonia is a very common respiratory tract infection in our country. Due to overcrowding and air pollution, the number of patients and hospitalization are increasing day by day. The assessment of disease severity and site of care decisions are very important for patients' safety and optimal use of resources. Late admission in the hospital or intensive care unit (ICU) leads to increased rate of mortality in CAP. Till now, several severity assessment scores are adopted throughout the world, but there is no study in our country regarding appropriate scoring for our population. So, this study aimed to identify the best scoring system from CURB-65, Expanded CURB-65, PSI and SMART-COP in the severity assessment of community acquired pneumonia.*

Patients and Methods: *This study was done in the Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka over a period of two year from July, 2018 to June 2020. It was a cross sectional analytical study. Patients admitted in this hospital with signs/symptoms of pneumonia like cough, haemoptysis, shortness of breath, chest pain, crackles on chest auscultation and consolidation in CXR were enrolled as the study population. Total 54 patients were found fulfilling the inclusion criteria. The outcome of the patients were recorded in terms of hospital stay, need for ICU admission and in hospital mortalily.*

Result: *At the end of the study, it was found that the median length of hospital stay was 8 days, intensive care unit (ICU) admission rate of CAP patients was 12(22.2%), mortality of CAP patients was 3(5.6%). Expanded CURB-65 score (5-8), SMART-COP score (5-9) and PSI class (V) were associated with more frequent ICU admission (66.7%) (n=8) in this study. Sensitivity and specificity in predicting ICU admission were 75.0% and 85.7% for CURB-65 (Ç2=17.14, df=1, p<0.001), 75.0% and 88.1% for Expanded CURB-65 (Ç2=19.34, df=1, p<0.001), 83.3% and 81.0% for SMART-COP (Ç2=17.35, df=1, p<0.001), 91.7% and 85.7% for PSI (Ç2=25.90, df=1, p<0.001) respectively. Sensitivity for predicting mortality was*

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100.0% in all scoring system and specificity of CURB-65 was 76.5% (Ç2=8.25, df=1, p-.004), 78.4% for Expanded CURB-65 (Ç2=9.07, df=1, p=.003), 70.6% for SMART-COP (Ç2=6.35, df=1, p=.012) and 72.5% for PSI (Ç2=6.91, df=1, p=.009). Among the four scoring, Expanded CURB-65 had best specificity both in predicting ICU admission and mortality of CAP.

Conclusion: *The present study concluded that Expanded CURB-65 score is simple, objective and more accurate scoring system for evaluation of CAP severity and can improve the efficiency of predicting ICU admission and mortality better than CURB-65, PSI and SMART-COP scores.*

Key words: *Pneumonia severity scoring, ICU admission, Sensitivity and specificity etc.*

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Introduction:

Pneumonia is a disease known to humanity from antiquity. It is an acute inflammation of the pulmonary parenchyma that can be caused by various infective and non-infective origins, presenting with physical and radiological features compatible with the pulmonary consolidation of a part or parts of one or both lungs.[1]Pneumonia is one of the leading causes of death and morbidity, both in developing and developed countries and is the commonest cause (10%) of hospitalization in adult and children. In United kingdom, 5–15% of patients hospitalized with community-acquired pneumonia (CAP) die within 30 days of admission, results in 29,000 deaths per annum and rising to 30% for those admitted to the intensive care unit.[2] In the United States, it is the fifth cause of death in people aged 65 and older.[3] Although in Bangladesh there are no available data that shows the burden of the disease in the adult population. The severity of the disease increases with the age as the elderly has concomitant co-morbidities. Irfan et al., (2009) showed that co-morbid illnesses were present in 63.5% patients with community acquired pneumonia in a developing country.[4]

Multiple serum biomarkers and several established evaluation scores have been used to assess the severity of CAP for improving management. Also predictors of mortality in individuals with CAP have been developed to identify at risk of poor outcomes early.[5,6] Pneumonia Severity Index (PSI) was the first scoring system, recommended by the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA).[7] PSI is composed of demographic variables, co-morbidities, physical exam/vital signs, and laboratory/imaging. It categorizes CAP patients into 5 classes (I,II,III,IV,V). Mortality and recommended site (outpatient, inpatient or ICU) of care can be obtained from PSI score.

Later, the British Thoracic Society recommended CURB-65 score for CAP management (Confusion, Blood Urea>7 mmol/L, Respiratory rate>30/min, Blood pressure-systolic<90 mm of Hg or diastolic<60 mm of Hg and Age over 65). It is used to determine the treatment criteria in outpatient, inpatient or ICU.[8] SMART-COP score (Systolic blood pressure, Multilobar infiltrates, Albumin, Respiratory rate, Tachycardia, Confusion, Oxygen saturation and Blood pH) was developed in Australia.[9] It can give better accuracy for prediction of the need for intensive respiratory or vasopressor support.

The Expanded CURB-65 is a modification of commonly used CURB-65 scoring system.[10] There are 3 additional markers (total 8) in the new scoring system which are Serum Albumin (<3.5 gm/L), Serum LDH (>230 u/L) and total platelet count (<100 x 10^9). S. Albumin, S. LDH and low platelet count are independent marker of pneumonia severity.[11,12,13] This assessment is divided into 3 classes according to the parameters. Class I>score 0-2=low risk (outpatient treatment), Class II>score 3-4=intermediate risk (inpatient treatment) and Class III>score 5-8=high risk (ICU treatment).It expands the independent risk factors into 8 variables in assessing CAP severity, significantly increases high-risk patient identification, through decreasing the relative weight of age and blood pressure, and excluding the use of imaging and

co-morbid illnesses in the calculation. This new scoring system is found to be more accurate for the severity classification in comparison with CURB-65 and PSI scores.[14]

In CURB-65, age is not a reliable marker for severity assessment in our country. For instance, many young patients are incorrectly categorized as low risk because of age less than 65 years, thus missing one point which reduces the scoring. Conversely the older patients above 65 years are sometimes falsely referring as severe. Also, many patients would be hypertensive, so low blood pressure will not be found frequently in severe CAP which also incorrectly reduces the severity score. Pneumonia severity index is determined by PORT prediction score which is composed of 20 variables. It is quite complicated, needs extensive investigations and time consuming to calculate, thus, limits regular clinical application. SMART-COP only emphasizes the need for ventilator/ vasopressor support in hospitalized patients. It does not categorize the patients of CAP for outpatient or inpatient management. This scoring also needs ABG analysis which is a sophisticated procedure and requires special analyzer which is not always available. The new Expanded CURB-65 scoring is simple which includes both the physical signs as well as important blood markers that can be done district level lab. So, this scoring is possible in the general medical practice, secondary or tertiary level hospital. Serum Albumin level and serum LDH are recognized marker of pneumonia severity. Septicemia and DIC can lead to low platelet count. Thus, addition of these three biomarkers in the existing CURB-65 scoring would be more accurate for early and proper management of complicated patients with special attention and by referring them to ICU when appropriate. This will reduce the financial burden, morbidity and mortality in Community Acquired Pneumonia. However, its effectiveness in Bangladesh setup has not been reported yet. That is why this study was done to see the superiority of this score comparing others.

Materials and methods:

This cross-sectional study was carried out in the Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka over a period of two year between July, 2018 to July 2020. Patients aged over 18 years attending in the hospital with the diagnosis of community acquired pneumonia based on two or more clinical signs and symptoms related to pneumonia (fever $>38^0$ C, cough, dyspnea, haemoptysis, chest pain or crackles on auscultation) and a chest radiograph showing feature of consolidation were the study population. Patients having pulmonary tuberculosis or respiratory fungal infection were excluded from this study. A total of 54 patients were enrolled meeting the inclusion and exclusion criteria. After taking written consent from each CAP patients, clinical examination (eg. Blood pressure, pulse, respiratory rate) and biochemical tests (Blood Urea, serum LDH, total platelet count, serum albumin etc.) were done and recorded. PSI, CURB-65, Expanded CURB-65 and SMART-COP scores were calculated. Finally, sensitivity, specificity, PPV and NPV were calculated for above scoring systems to predict ICU admission and mortality. Statistical analysis was done by SPSS (Statistical Package for Social Sciences) software version 22. Numerical data were presented as mean with standard deviation and categorical data were presented as frequency & their percentage. A p value <0.05 was considered statistically significant. The summarized data were present in the table.

Results:

Table-I

Demographic profile of the study subjects (N=54)

	Frequency (n)	Percentage
Age (years)		
≤30	13	24.1
31 - 50	19	35.2
>50	22	40.8
Mean ±SD	46.74 ± 18.98	
Gender		
Male	40	74.1
Female	14	25.9
Residence		
Urban	34	62.96
Rural	20	37.04

Table I shows maximum patients were >50 years old followed by 35.2% in age group 31-50 years and 24.1% ≤30 years. Mean age of the study subjects was 46.74 ± 18.98 years. Males (74.1%) were predominant than females (25.9%) and male to female ratio was 2.85:1. 62.96% patients were urban people and 37.04% patients were from rural area.

Table-II

Clinical profile of the study subjects (N=54)

	Frequency (n)	Percentage
GCS [Mean ±SD]	14.44 ± 1.30	
Respiratory rate(≥30/min)	26	48.1
Respiratory rate (/min) [Mean ±SD]	29.24 ± 4.00	
Systolic BP (mm of Hg) [Mean ±SD]	116.59 ± 17.78	
Diastolic BP (mm of Hg) [Mean ±SD]	71.30 ± 9.12	
SBP<90 or DBP ≤60	11	20.4
Heart rate (/min)[Mean ±SD]	78+13.4	

Table-III

Laboratory investigation findings of the study subjects (N=54)

	Mean ±SD	Min - max
Blood urea (mmol/L)	6.09 ± 3.55	1.85 - 22.00
High blood Urea (>7mmol/L)	14 (25.92%)	
Total platelet count	276074 ± 123355	41000 – 596000
Thrombocytopenia(<1,50,000/μL)	4 (7.4%)	
Serum LDH (U/L)	512.50 ± 317.83	119 – 1560
High serum LDH (>230 U/L)	46 (85.2%)	
Serum Sodium (mmol/L)	138.65 + 6.79	107- 150
Hyponatremia (<135 mmol/L)	8 (14.81%)	
Serum Potassium (mmol/L)	4.1 + .6	2.4-6.1
Hypokalemia (mmol/L)	5 (9.26%)	
Serum albumin (g/dl)	3.35 ± 0.73	1.90 - 6.20
Hypoalbuminemia, (<3 g/dl)	29 (53.7%)	
Sputum C/S (growth)	10 (18.15%)	

Table II shows mean GCS was 14.44 + 1.30, mean respiratory rate was 29.24 ± 4.00 /min and 48.1% of the study subjects had respiratory rate e"30/ min. 20.4% of the study subjects had SBP<90 or DBP d"60.Mean heart rate was 78+13.4/min.

Table III shows mean value of blood urea, platelet count, serum albumin, serum LDH were 6.09 ± 3.55 mmol/L, 276074 ± 123355, 3.35 ± 0.73 g/dl and 512.50 ± 317.83 U/L respectively. Culture of sputum was positive in 18.15% cases. High blood Urea was found in 25.92 % cases, high serum LDH was in 85.2% cases, thrombocytopenia was in 7.4% cases and hypoalbuminemia in 53.7% cases. Hyponatremia was found in 14.81% and hypokalemia in 9.26%.

Table-IV

Distribution of patients according to management output at hospital ward

	Frequency (n)	Percentage
ICU admission	12	22.2
Length of hospital stay in days [Mean ±SD]	8.16 ± 3.41	
Mortality	3	5.6

Table IV shows intensive care unit (ICU) admission rate of CAP patients was 22.2%, the median length of hospital stay was 8 days. The overall mortality rate was 5.6%.

Table-V

Distribution of the study subjects according to the grading of different scoring systems (N=54)

	Frequency (n)	Percentage
CURB-65 score		
0 – 1 (PP-OPD)	39	72.2
2 – 3 (PP-IPD)	14	25.9
4 – 5 (PP-ICU)	1	1.9
Expanded CURB-65 score		
0 – 1 (PP-OPD)	20	37.0
2 – 4 (PP-IPD)	23	42.6
5 – 8 (PP-ICU)	11	20.4
SMART-COP score		
0 – 1 (PP-OPD)	23	42.6
2 – 4 (PP-IPD)	20	37.0
5 – 9 (PP-ICU)	11	20.4
PSI score		
Class I –II (PP-OPD)	24	44.4
Class III-IV (PP-IPD)	20	37.1
Class V (PP-ICU)	10	18.5

(PP-OPD= Patient predicted for outpatient management, PP-IPD= Patient predicted for inpatient management, PP-ICU= Patient predicted for intensive care unit management)

Table V shows distribution of the study subjects according to different scoring systems. High risk was similar in Expanded CURB, SMART-COP and PSI scoring. According to CURB-65 score, 72.2% patients were suggested for outpatient treatment, 25.9% inpatient and 1.9% ICU; according to Expanded CURB-65 score, 37.0% patients were suggested for outpatient treatment, 42.6% inpatient and 20.4% ICU; according to SMART-COP score, 42.6% patients were suggested for outpatient treatment, 37.0% inpatient and 20.4% ICU; according to PSI score, 44.4% patients were suggested for outpatient treatment, 37.1% inpatient and 18.5% ICU.

(PP-OPD= Patient predicted for outpatient management, PP-IPD= Patient predicted for inpatient management, PP-ICU= Patient predicted for intensive care unit management)

Table VI shows different initial scores of 12 patients who later got admitted in the ICU. Of them 25.0% were predicted to be treated in outpatient setting, 66.7% in inpatient and 8.3% in ICU according to CURB-65 score. 8.3% were suggested to be treated in outpatient setting, 25.0% in inpatient and 66.7% in ICU according to Expanded CURB-65 score. 8.3% were suggested to be treated in outpatient setting, 25.0% in inpatient and 66.7% in ICU according to

Table-VI

Distribution of severity scoring systems during admission in patients required ICU management (N=12)

	CURB-65	ExpandedCURB-65	SMART-COP	PSI
Outpatient(PP-OPD)	3 (25.0%)	1 (8.3%)	1 (8.3%)	0 (0.0%)
Inpatient(PP-IPD)	8 (66.7%)	3 (25.0%)	3 (25.0%)	4 (33.3%)
ICU(PP-ICU)	1 (8.3%)	8 (66.7%)	8 (66.7%)	8 (66.7%)

Table-VII

The accuracy of different scoring systems in predicting ICU admission (N=12)

Scoring system	Threshold	$Ç^2$	df	p-value	Sensitivity	Specificity	PPV	NPV
CURB-65	≥2	17.14	1	<0.001	75.0	85.7	60.0	92.3
Expanded CURB-65	≥4	19.34	1	<0.001	75.0	88.1	64.3	92.5
SMART-COP	≥4	17.35	1	<0.001	83.3	81.0	55.6	94.4
PSI	≥4	25.90	1	<0.001	91.7	85.7	64.7	97.3

(Chi-square test was done to measure the level of significance. For CURB-65, $Ç^2$ = 17.14 with df=1 and p-value <0.001. For Expanded CURB-65, $Ç^2$ = 19.34 with df=1 and p value<0.001. For SMART-COP, $Ç^2$ = 17.35 with df=1 and p-value<0.001. For PSI, $Ç^2$ = 25.90 with df=1 and p-value<0.001)

Table-VIII

Distribution of the severity scoring systems during admission who died in the hospital (N=3)

	CURB-65	ExpandedCURB-65	SMART-COP	PSI
Outpatient(PP-OPD)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Inpatient(PP-IPD)	3(100%)	0 (0.0%)	1 (33.3%)	2(66.7%)
ICU(PP-ICU)	0 (0.0%)	3 (100.0%)	2 (66.7%)	1 (33.3%)

(PP-OPD= Patient predicted for outpatient management, PP-IPD= Patient predicted for inpatient management, PP-ICU= Patient predicted for intensive care unit management)

Table-IX

The accuracy of different scoring systems in predicting mortality (N=3)

Scoring system	Threshold	$Ç^2$	df	p-value	Sensitivity	Specificity	PPV	NPV
CURB-65	≥2	8.25	1	0.004	100.0	76.5	20.0	100.0
Expanded CURB-65	≥4	9.07	1	0.003	100.0	78.4	21.4	100.0
SMART-COP	≥4	6.35	1	0.012	100.0	70.6	16.7	100.0
PSI	≥4	6.91	1	0.009	100.0	72.5	17.6	100.0

(Chi-square test was done to measure the level of significance. For CURB-65, $Ç^2 = 8.25$ with df=1 and p-value=0.004. For Expanded CURB-65, $Ç^2 = 9.07$ with df=1 and p value=0.004. For SMART-COP, $Ç^2 = 6.35$ with df=1 and p-value=0.012. For PSI, $Ç^2 = 6.91$ with df=1 and p-value=0.009)

SMART-COP score. 33.3% were predicted to be treated in inpatient and 66.7% in ICU were according to PSI score.

Table VII shows accuracy of different scoring systems in predicting ICU admission. Among four scoring, PSI had better sensitivity but Expanded CURB-65 had better specificity. Sensitivity, specificity, PPV and NPV were 75.0%, 85.7%, 60.0% and 92.3% respectively according to CURB-65 score at a cutoff value 2; sensitivity, specificity, PPV and NPV were 75.0%, 88.1%, 64.3% and 92.5% respectively according to Expanded CURB-65 score at a cutoff value 4; sensitivity, specificity, PPV and NPV were 83.3%, 81.0%, 55.6% and 94.4% respectively according to SMART-COP score at a cutoff value 4; sensitivity, specificity, PPV and NPV were 91.7%, 85.7%, 64.7% and 97.3% respectively according to PSI score at a cutoff value 4 in predicting ICU admission. UK guidelines on admission to and discharge from intensive care and high dependency units (1996) protocol was taken as the gold standard for predicting severely ill patients who needed ICU admission.

Table VIII shows different initial scores in 3 patients who later died in the hospital.. Of them, all were suggested to be treated in inpatient setting according to CURB-65 score; all were suggested to be treated in ICU according to Expanded CURB-65 score; 33.3% were suggested to be treated inpatient and 66.7% in ICU according to SMART-COP score; 66.7% inpatient and 33.3% in ICU according to PSI score.

Table 4.9 shows accuracy of different scoring systems in predicting mortality. Among four scoring, Expanded CURB-65 had better sensitivity & specificity. Sensitivity, specificity, PPV and NPV were 100.0%, 76.5%, 20.0% and 100.0% respectively according to CURB-65 score at a cutoff value 2; sensitivity, specificity, PPV and NPV were 100.0%, 78.4%, 21.4% and 100.0% respectively according to Expanded CURB-65 score at a cutoff value 4; sensitivity, specificity, PPV and NPV were 100.0%, 70.6%, 16.7% and 100.0% respectively according to SMART-COP score at a cutoff value 4; sensitivity, specificity, PPV and NPV were 100.0%, 72.5%, 17.6% and 100.0% respectively according to PSI score at a cutoff value 4 in predicting mortality. UK guidelines on admission to and discharge from intensive care and high dependency units (1996) protocol was taken as the gold standard for predicting severely ill patients who needed ICU admission.

Discussion:

In this study, maximum patients were >50 years old followed by 35.2% in age group 31-50 years and 24.1% d" 30 years. Mean age of the study subjects was 46.74±18.98 years. Mean age was comparatively higher in other studies.[14,15] Males (74.1%) were predominant than females (25.9%) and male to female ratio was 2.85:1. Male predominance was also observed in other studies.[14,15]Mean respiratory rate was 29.24 ± 4.00 /min and 48.1% of the study subjects had respiratory rate ≥30/min. 62.0% patients had respiratory rate ≥30/min.[14] 20.4% of the study subjects had SBP<90 or DBP ≤60. 36.8% patients had SBP<90 or DBP ≤60.[14]In the study of Shindo et al., (2008) 30.7% patients had SBP<90 or DBP ≤60.[15]

Mean value of blood urea, platelet count, serum albumin, serum LDH were 6.09 ± 3.55 mmol/L, 276074 ± 123355, 3.35 ± 0.73 g/dl and 512.50 ± 317.83 U/L respectively. High serum LDH was found in 85.2% cases, thrombocytopenia was in 7.4% cases and hypoalbuminemia in 53.7% cases. Hyponatremia was found in 14.81% and hypokalemia was in 9.26% patients. In the study of Shehata et al., (2017) high LDH was in 44.8% cases, thrombocytopenia in 22.8% cases and hypoalbuminemia was in 33.2% cases.[14]

As regards patients' outcomes, it was found that intensive care unit (ICU) admission rate of CAP patients was 22.2% and the median length of hospital stay was 8 days. The overall mortality rate was 5.6%. Shehata et al., (2017) found in their study that ICU admission rate of CAP patients was 29.6%, the median length of hospital stay was 8 days and 30-day mortality rate was 11.2%.[14] Irfan et al., (2009) found that the overall mortality in their study population was 11%.[4] On the other hand, Zhang et al., (2016) found that the overall 30-day mortality rate was 15.7%, Intensive care unit (ICU) admission rate was 5.8% and the median length of hospital stay was four days.[16] Also, Liu et al., (2016) concluded that the median length of stay (LOS) was 10 day and the 30-day mortality was 8.48%.[10] Buising et al., (2006) and Shah et al., (2010) stated that ICU admission rates were 6.6% and 23.3%, respectively.[17,18] Shindo et al., (2008) found 30-day mortality (9.4%), ICU admission (14.6%) and median length of hospital stay 13 days.[15]

Expanded CURB-65 score (5-8), SMART-COP score (5-9) and PSI class (V) were associated with more frequent ICU admission (66.7%) in this study. So, expanded CURB-65, SMART-COP and PSI scores can identify the severe CAP patients who need ICU admission, better than CURB-65 score. Expanded CURB-65 score (5–8) was associated with more frequent ICU admission about 49.4% than PSI class (IV-V) and CURB-65 score (3–5) (Shehata et al., 2017).[14] Charles et al., (2008) suggested that neither PSI nor CURB-65 was designed to identify patients who need ICU referral.[9]

In predicting ICU admission, sensitivity of CURB-65, Expanded CURB-65, SMART-COP and PSI were 75.0%, 75.0%, 83.3% and 91.7%. Specificity of CURB-65, Expanded CURB-65, SMART-COP and PSI were 85.7%, 88.1%, 81.0% and 85.7% respectively. Among four scoring, PSI had better sensitivity but Expanded CURB-65 had better specificity. In this study of Shehata et al., (2017), the sensitivity of the Expanded CURB-65 score for prediction of ICU admission was higher than other two scores (p-value 0.0003).[14] So the Expanded CURB-65 score was better than the other two scores in predicting the severe patients who needed ICU admission.

In predicting mortality, sensitivity was 100.0% in all scoring systems. Specificity of CURB-65, Expanded CURB-65, SMART-COP and PSI were 76.5%, 78.4%, 70.6% and 72.5% respectively. Among four scoring, Expanded CURB-65 had better specificity. The study of Shehata et al., (2017) demonstrated that the Expanded CURB-65 score gave the most sensitive prediction of mortality (75%) with the highest NPV (95.9%).[14] The Expanded CURB-65 scoring system was the best predictor of 30-day mortality in CAP patients as it had the largest AUC (0.793) p-value < 0.0001). These results were comparable with other study in which the overall sensitivity and specificity of expanded-CURB-65 were superior (AUC = 0.826) to other score systems, of which the AUCs were 0.801, 0.756 for PSI, CURB-65 respectively in predicting the 30-day mortality.[10]

So among the four scoring, Expanded CURB-65 had better specificity in predicting ICU admission and mortality.

Limitation of the study:

Small sample size is the main limitation of the study. Also the study should be done in the outpatient department which would give the prediction of hospitalization for different scoring. Some patient received antibiotic prior admission to this hospital which might interfere the outcome of the patients.

Conclusion:

Pneumonia Severity Index or PSI is used to predict the mortality of CAP, but its complexity and extensive investigations limits its use in outpatient setting. SMART-COP scoring is used for hospital admitted patient who require vasopressor or mechanical ventilation. CURB-65 is easier but too simple and less reliable for identifying high risk patient. On the other hand, Expanded CURB-65 is objective, more accurate in categorizing the patients for outpatient treatment, hospital care or ICU support. It can be done at GP level, specialist chamber or hospital setting. It also improves the efficiency of predicting mortality in CAP patient better than CURB-65, PSI or SMART-COP scoring.

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ORIGINAL ARTICLE

Association of Serum Magnesium with Sputum Smear Conversion at the end of 2nd month among Smear Positive Pulmonary Tuberculosis Patients

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Abstract

Background: *The progress of an infectious condition is partly affected by the overall nutrition of the host. Many of the essential trace elements like zinc, copper, magnesium influence the function of the immune system. Magnesium levels also influence tuberculosis. Tuberculosis and malnutrition is well recognized to go hand in hand as one can lead to the other.*

Methods: *This prospective observational study was conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from July 2018 to June 2020. A total of 85 new smear positive pulmonary tuberculosis cases were enrolled in this study. Serum Magnesium was measured by the colorimetric method using Xylidyl Blue-I. Statistical analyses of the results were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-23).*

Results: *In this study 74(87.1%) patients had sputum smear conversion and 11(12.9%) had delayed sputum smear conversion at the end of intensive phase of treatment. Mean initial serum magnesium was 1.95±0.26 mg/dl and mean serum magnesium at the end of 2nd month was 2.07±0.24 mg/dl. Significant association was found in sputum smear conversion with smoking, initial serum magnesium level and serum magnesium level at the end of 2nd month. There was no significant association of sputum smear conversion with diabetes mellitus and BMI. In multivariate logistic regression analysis, initial low serum magnesium level and smoking were found to be independent predictors for sputum smear non-conversion at the end of 2nd month but low serum magnesium at the end of 2nd month was not found to be independent predictor for sputum smear non-conversion.*

Conclusion: *Hypomagnesaemia at the initiation of anti-tubercular therapy was significantly associated with sputum smear non-conversion at the end of intensive phase of treatment.*

Key words: *Smear positive pulmonary tuberculosis, Smear conversion, Serum magnesium*

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Introduction:

Worldwide, tuberculosis is the leading cause of death from a single infectious agent. Millions of people continue to fall sick with TB each year. In 2017, TB caused an estimated 1.3 million deaths (range, 1.2–1.4 million) among HIV-negative people and there were an additional 300000 deaths from TB (range, 266000–335000) among HIV-positive people.[1] Tuberculosis is a curable and preventable disease caused by infection with mycobacteria from the Mycobacterium tuberculosis complex.[2] Magnesium is the eight common element in the crust of earth, fourth most abundant cation in human body and second abundant intracellular cation. It may exist as protein bound, complexed or in free form. It is primarily found within the cell, where it acts as a counter ion for the energy-rich ATP and nuclear acids. It is a cofactor in more than 300 enzymatic reactions. Magnesium critically stabilizes enzymes, including many ATP generating reactions.[3] It is also key component in various reactions that require kinases and important factor in both cellular and humoral immune reactions .[4,5] Magnesium participates in immune responses in numerous ways: as a cofactor for immunoglobulin synthesis, C'3 convertase, immune cell adherence, antibody-dependent cytolysis, IgM lymphocyte binding, macrophage response to lymphokines, T helper-B cell adherence, binding of substance P to lymphoblasts and antigen binding to macrophage RNA.[6]

The development of tuberculosis passes through several distinct stages-initial infection, entry of the pathogen into tissues and cells, survival and replication within macrophages, subversion of immune defense mechanisms, establishment of dormancy, reactivation from the latent state and induction of gross tissue necrosis that is responsible for cavitary formation, entry of bacilli into the sputum and transmissibility of infection. The progression of the disease process to resolution and healing or to progression with extensive necrosis is determined by the nature of the host immune system.[7]

Hypomagnesaemia promotes low-grade inflammation as demonstrated by elevated concentrations of C-Reactive Protein (CRP) and TNF-alpha.[8,9] Mg improves markers of inflammation and oxidative stress.[10] Irfan et al. observed that, a significant inverse relationship was observed between the level of serum magnesium with duration of illness and extent of the disease.[11] Memon et al. concluded that decreased serum magnesium is an important finding in pulmonary tuberculosis patient.[12] Agrawal et al. showed that lower serum magnesium level at the initiation of tuberculosis therapy was significantly associated with delayed sputum conversion among smear positive pulmonary tuberculosis patients.[13] That's why one needs to find out the association of serum magnesium level with delaying the sputum conversion in order to lay the foundation of effective intervention in our country. The main objective of this study is to find out the association of serum magnesium with sputum smear conversion at the end of 2nd month among smear positive pulmonary tuberculosis patients.

Methods:

This prospective observational study was carried out in the Department of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during the period from July 2018 to June 2020. New cases of sputum smear positive pulmonary tuberculosis patient aged e" 18 years who attended in NIDCH both indoor & outdoor and who gave informed consent were enrolled in this study. MDR TB, XDR TB, CAT -1 failure, retreatment case, pregnancy, chronic renal failure and patient with long term corticosteroid therapy were excluded from the study. A total of 95 new smear positive pulmonary tuberculosis patients attending in the above hospital were included in this study. Among them 10 (7 patients were lost to follow up and 3 were died) patients were excluded from this study. Finally 85 patients were enrolled in the study. Having obtained ethical clearance from the Ethical Committee and informed written consent from the patients, the data collection was commenced. All patients were subjected to detailed history taking, physical examination and necessary investigations. Investigations included complete blood count, random blood sugar, sputum for AFB, chest x-ray, s. creatinine, SGPT, Sputum for Gene Xpert and serum magnesium level. Patients were treated by Cat-1 anti TB treatment. At the end of 2nd month of treatment all patients were followed up clinically and sputum for AFB and serum magnesium were done. Serum Mg levels were measured by the colorimetric method using Xylidyl Blue - I. The collected data of each patient was recorded systematically. All data were analyzed by using computer based SPSS -23 (statistical package for social sciences). Data were presented in frequency, percentage and mean and standard deviation as

applicable. Chi square test was used for categorical variables. Unpaired t-test was used for continuous variables as shown cross tabulation. Multivariate logistic regression analysis was used for sputum smear non-conversion and the results were expressed as odds ratios with 95% confidence intervals (CI). P value of less than 0.05 was considered as statistically significant.

Results:

Table-I

Demographic characteristics of the study patients (n=85)

Demographic characteristics	Number of patients	Percentage
Age (years)		
≤20	2	2.4
21-40	42	49.4
41-60	40	47.1
>60	1	1.2
Mean age (years)	40.0±12.5	
Range (min-max)	19.0-70.0	
Sex		
Male	72	84.7
Female	13	15.3

Table II

Distribution of serum magnesium among the study patients (n=85)

Serum magnesium (mg/dl)	Mean±SD
Initial	1.95±0.26
Range (min-max)	1.1-2.55
At the end of 2nd month	2.07±0.24
Range (min-max)	1.35-2.6

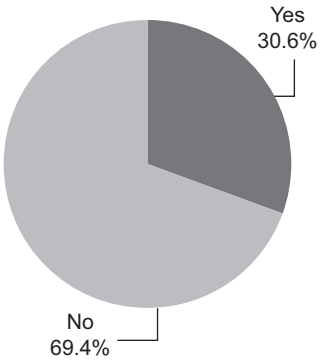

Fig.-1: *Pie chart showing smoker among the study patients*

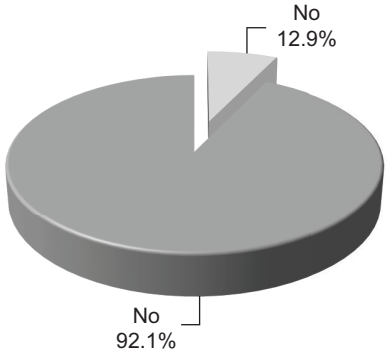

Fig.-2: *Pie chart showing diabetes mellitus among the participants*

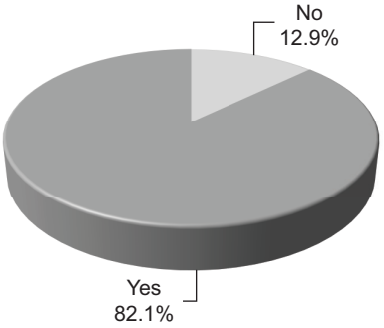

Fig.-3: *Pie chart showing sputum smear conversion at the end of 2nd month*

Table-III

Association between diabetes mellitus and sputum smear conversion (n=85)

Diabetes mellitus	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
Yes	2	18.2	4	5.4	0.123ns
No	9	81.8	70	94.6	

(ns= not significant; p value reached from chi square test)

Table-IV

Association between smoking and sputum smear conversion (n=85)

Smoker	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
Yes	7	63.6	19	25.7	0.017[s]
No	4	36.4	55	74.3	

(s= significant; p value reached from chi square test)

Table-V

Association between initial BMI and sputum smear conversion (n=85)

BMI (kg/m^2)	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
<18.5	6	54.5	18	24.3	
18.5-24.9	5	45.5	53	71.6	0.105[ns]
≥25.0	0	0.0	3	4.1	

(ns= not significant; p value reached from chi square test)

Table-VI

Association between BMI at the end of 2nd month and sputum smear conversion (n=85)

BMI (kg/m^2)	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
<18.5	4	36.4	16	21.6	
18.5-24.9	7	63.6	54	73.0	0.450[ns]
≥25.0	0	0.0	4	5.4	

(ns= not significant; p value reached from chi square test)

Table-VII

Association between initial serum magnesium level and sputum smear conversion (n=85)

Initial serum magnesium (mg/dl)	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
<1.82	10	90.9	12	16.2	
1.82-2.43	1	9.1	60	81.1	
>2.43	0	0.0	2	2.7	
Mean±SD	1.53	±0.24	2.01	±0.19	0.001[s]

(s= significant; p value reached from unpaired t-test)

Table-VIII

Association between serum magnesium level at the end of 2nd month and sputum smear conversion (n=85)

Serum magnesium at the end of 2nd month (mg/dl)	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
<1.82	8	72.7	7	9.4	
1.82-2.43	3	27.3	64	86.5	
>2.43	0	0.0	3	4.1	
Mean±SD	1.69	±0.19	2.13	±0.20	0.001[s]

(s= significant; p value reached from unpaired t-test)

Table-IX

Multivariate regression analysis for sputum smear non-conversion (n=85)

Variable	Adjusted OR	95% CI		P value
		Lower	Upper	
Smoking	7.377	1.038	52.451	0.046[s]
Initial low serum magnesium level	37.648	3.081	99.087	0.004[s]
Low serum magnesium level at the end of 2nd month	4.517	0.682	29.894	0.118[ns]

(s= significant, ns= not significant, OR=Odd's Ratio; p value reached from multivariate logistic regression analysis)

Discussion:

Early diagnosis and effective treatment of TB remains the key to success for infection control. For assessment of outcome of TB treatment, sputum smear microscopy at two month of DOTS treatment is a very important parameter.[13]

This prospective observational study was carried out with an aim to determine the serum magnesium level in smear positive pulmonary tuberculosis patients and to observe the smear conversion at the end of 2nd month of anti-tubercular therapy. This study also finds out find out any association of serum magnesium status in non-converter patients. In this study it was observed that almost half (49.4%) of the patients belonged to age 21-40 years. The mean age was found 40.0±12.5 years with range from 19 to 70 years. Almost similar study conducted by Guler et al. which showed the mean age was found 42.8±16.4 years.[14] In the present study it was observed that majority 72(84.7%) patients were male and 13(15.3%) were female. Male to female ratio was 5.5:1. In a study Agrawal et al. which showed most participants (67%) were male and 33.0% were female.[13] This study showed more than two third (68.2%) patients had initial BMI 18.5-24.9 kg/m^2, 24(28.2%) had <18.5 kg/m^2 and 3(3.5%) had e"25.0 kg/m^2. Almost three fourth (71.8%) patients had BMI 18.5-24.9 kg/m^2, 20(23.5%) had <18.5 kg/m^2 and 4(4.7%) had e"25.0 kg/m^2 at the end of 2nd month.

In this current study it was observed that 26(30.6%) patients were smoker and 59(69.4%) were non-smoker. Bouti et al. documented that smoker was 36.1%.[15] Another study reported by Azarkar et al. which showed smoker was 14(16.5%).[16] In this study it was observed that only 6(7.1%) patients had diabetes mellitus.

In this study it was observed that 74(87.1%) patients had sputum conversion at the end of 2nd month. Ndubuisi et al. found sputum conversion rate among new smear positive pulmonary tuberculosis patients at the end of 2nd month post therapy was 86.9%.[17] Kuaban et al. also showed similar results.[18]

In this study it was observed that mean initial serum magnesium was found 1.95±0.26 mg/dl with range from 1.1 to 2.55 mg/dl. The mean serum magnesium at the end of 2nd month was found 2.07±0.24 mg/dl with range from 1.35 to 2.6 mg/dl.

Irfan et al. reported that serum magnesium was 1.633±0.065 mg/dl.[11] Another study documented by Memon et al. where they found serum magnesium was 1.21±0.083 mg/dl.[12]

In this present study it was observed that 2(18.2%) patients had diabetes mellitus in sputum non-conversion and 4(5.4%) in sputum conversion group. The difference were not statistically significant ($p>0.05$) between two group. In my study it was observed that 7(63.6%) patients were smoker in sputum delayed conversion group and 19(25.7%) in sputum conversion group. The difference were statistically significant ($p<0.05$) between two group. Metanat et al. narrated that there was a significant delay in sputum conversion time between smoker and non-smoker.[19] Anandaraj et al. described smoking was significantly associated with delayed sputum smear conversion at the end of intensive phase.[20]

In this current study it was observed that initial BMI <18.5 kg/m^2 was found 6(54.5%) patients in sputum not conversion and 18(24.3%) in sputum conversion group. The difference was not statistically significant ($p>0.05$) between two group. At the end of 2nd month, BMI 18.5-24.9 kg/m^2 was found 7(63.6%) patients in sputum non-conversion and 54(73.0%) in sputum conversion group. The difference was not statistically significant ($p>0.05$) between two group.

Our study showed that mean initial serum magnesium was found 1.53±0.24 mg/dl in sputum non-conversion and 2.01±0.19 mg/dl in sputum conversion group. The difference were statistically significant ($p<0.05$) between two group. The mean serum magnesium at the end of 2nd month was found 1.69±0.19 mg/dl in sputum non- conversion and 2.13±0.20 mg/dl in sputum conversion group. The difference was statistically significant ($p<0.05$) between two group. Delayed sputum smear conversion occurred in 11(12.94%) sputum smear positive PTB patients. Among them 10 delayed sputum smear conversion patient had initial serum magnesium levels <1.8 mg/dl and 8 had serum magnesium levels < 1.8 mg/dl at the end of 2nd month. In the study Memon et al. (2014) described that serum magnesium was found significantly lower in patients as compared with the controls.[12] In the study Agrawal et al. showed that lower serum magnesium level at the initiation of tuberculosis therapy was significantly associated with delayed sputum conversion among smear positive pulmonary tuberculosis patients.[13]

In multivariate logistic regression analysis, initial low serum magnesium level and smoking were found to be independent predictors for sputum smear non-conversion at the end of 2nd month. Among the predictors, initial low serum magnesium level was the strongest predictor of sputum smear non-conversion. However, low serum magnesium level at the end of 2nd month was not found to be independent predictor for sputum smear non-conversion at the end of intensive phase of the treatment.

Conclusion

Initial low serum magnesium level was significantly associated with sputum smear non-conversion at the end of 2nd month. The underlying mechanism responsible for the association of initial low magnesium level with significant delay in the sputum smear conversion yet to be discovered.

Conflict of Interest: The authors of this paper have declared that there is no conflict of interest to any of the authors.

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ORIGINAL ARTICLE

Risk Factors for Multidrug Resistant Organisms in Exacerbation of Bronchiectasis

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Abstract:

Background & Objective: *Bronchiectasis is a chronic debilitating airway disease. Patients with bronchiectasis are prone to repetitive infective exacerbations. Antibiotics are considered the cornerstone in the management of exacerbations. Frequent treatment with antibiotics makes the organism much more susceptible to acquire antibiotic resistance that account for a substantial number of excess deaths and catastrophic healthcare spending. Attention in focusing the risk factors for antibiotic resistance is necessary to take steps to reduce the development of resistant organisms and framing antibiotic policy.*

Patients & Methods: *This cross-sectional observational and analytical study was conducted in the Inpatient Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from April 2019 to April 2020. A total of 202 adult patients with exacerbation of bronchiectasis were enrolled. Early morning Sputum were examined for bacteriological culture and sensitivity. Multidrug-resistance was determined according to European Centre of Disease Prevention and Control classification.*

Result: *Two hundred and two exacerbations were included and microorganisms were isolated in 155 cases.* Pseudomonas aeruginosa *87(55.8%) and* Klebsiella pneumoniae *53(34.0%) were more frequent. Multidrug-resistant pathogens were found in 90(58.1%) cases. In multivariate analysis, recent hospitalization (Odds ratio (OR)2.42,95% CI 1.03-5.71), frequent antibiotic use (OR 2.650, 95% CI 1.21-5.80) and chronic kidney disease (5.98,95%CI 1.57-22.81) were found to be independent predictors for MDR pathogens.*

Conclusion: *Recent hospitalization, frequent antibiotic use and chronic kidney disease were seemed to be the risk factor for multidrug resistant bacteria. Identification of the factors associated with antibiotic resistance helps in rational prescription of antibiotics.*

Key words: *Multidrug Resistant Organism, exacerbation of Bronchiectasis, risk factors*

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Introduction:

Bronchiectasis is defined as an abnormal and permanent dilatation of one or more bronchi.[1] It is a chronic respiratory disease presenting with chronic cough and sputum production, some have hemoptysis and shortness of breath. Increased production of mucous together with impaired mucociliary clearance leads to accumulation of secretion in dilated bronchi and causes recurrent respiratory infections. A vicious cycle is established involving persistent bacterial colonization, chronic inflammation of the bronchial mucosa, airway damage and remodeling. In most cases, infection is the primary force behind this ongoing cycle.[2]

Patients with bronchiectasis are prone to frequent exacerbations which have traditionally been viewed as being exclusively bacterial, evidenced by epidemiological data. So, identification and appropriate treatment of these organisms is an essential part of the management of bronchiectasis. Bacteria most commonly isolated from the airways of patients with bronchiectasis include *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Moraxella catarrhalis*.[3] Dominant bacteria are *Pseudomonas aeruginosa* and *Haemophilus influenza* worldwide.[4]

Antibiotics aiming to treat bacterial infections of the respiratory tract, or to control bacterial colonization, or both, represent a central component of the treatment of bronchiectasis. Those having frequent exacerbations causing significant morbidity, antibiotic therapy appears to decrease the frequency and severity of exacerbations at the expense of emerging drug resistance.[5]

Optimal antibiotic use is crucial, especially in an era of rising antibiotic resistance and lack of new antimicrobial development.[6] Over-prescribing and mal-prescribing of antibiotics are undoubtedly contributing to the growing challenges posed by antibiotic resistant bacteria, and epidemiological studies have clearly demonstrated direct relationships between antibiotic consumption and the emergence and dissemination of resistant strains.[7]

Leaders in world health have described antimicrobial-resistant bacteria as "nightmare bacteria" that account for a substantial number of excess deaths and catastrophic healthcare spending[8]. The impact of antibiotic resistant bacteria is suggested to be far more serious in low- and middle-income countries (LMICs) than in well-resourced countries.

Routine screening is vital due to the circulation of resistant organisms in the community. Attention to identify the risk factors for antibiotic resistance is necessary to take steps to prevent the development of resistant organisms and framing antibiotic policy.

Materials and Methods:

This cross-sectional analytical study was carried out in the Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka over a period of one year between April 2019 to April 2020. Adult patients presented with exacerbation of bronchiectasis admitted to the inpatient Department of Respiratory Medicine were the study population. Patients with concomitant pulmonary tuberculosis were excluded from the study. A total of 202 cases were taken in the study. Study samples were selected by purposive sampling.

Having obtained ethical clearance from the Ethical Committee and verbal consent from the patients, the data collection was commenced. Statistical analyses were carried out using Statistical Package for Social Sciences, version 23.0. Data were presented in frequency, percentage and mean and standard deviation as applicable. Chi square test was used for categorical variables. Univariate and Multivariate logistic analysis were used for risk factors. For all analytical tests, the level of significance was set 5% and p-value < 0.05 was considered significant. The findings obtained from data analyses are presented below:

Results:

A total of 202 patients with exacerbation of bronchiectasis including 126 males (62.4%) and 76 females (37.6%) with a mean age of 47.2 years (range 19 - 83 years) who were admitted in department of respiratory medicine, NIDCH entered the study.

Among study population, 92(45.5%) were Diabetic, 34(16.8%) had chronic kidney disease, 97(48.0%) were smoker and 178(88.1%) from rural area.178(88.1%) cases had previous exacerbation,

103(51.0%) had history of recent hospitalization, frequent antibiotic user were122(60.4%), 87(43.1%) had history of previous I/V antibiotics, 16(7.9%) had previous ICU admission, 30(14.9%) had previous isolation of resistant organism and use of immunosuppressive drugs were 6(3.0%) .

Sputum for C/S showed bacterial growth in 155(76.7%) with multidrug-resistant organism in 90 (58.1%) cases.

In univariate analysis, previous exacerbation, recent hospitalization, frequent antibiotic use, diabetes mellitus and chronic kidney disease were found to be independent predictors for MDR pathogens.

In multivariable analysis, recent hospitalization, frequent antibiotic use and chronic kidney disease were found to be independent predictors for MDR pathogens.

Table I.

Demographic Characteristics of the Study Cases (n=202)

Demographic characteristic	Number of patients	Percentage
Sex		
Male	126	62.4
Female	76	37.6
Mean age (years)	47.2	±16.3
Range (min-max)	19.0	-83.0
Residence		
Rural	178	88.1
Urban	24	11.9
Smoker		
Yes	97	48.0
No	105	52.0

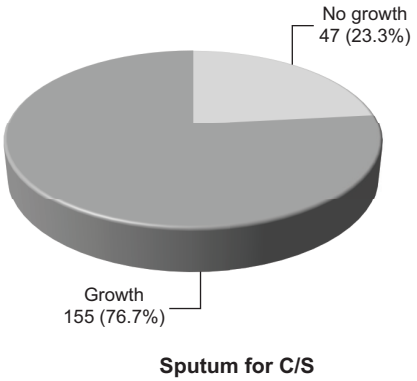

Fig.-1: *Distribution of the Study Cases According to Culture of Bacteria*

Table-II

Distribution of the Study Cases According to Growth of the Bacteria (n=155)

Name of the bacteria	Number of patients	Percentage
Pseudomonas aeruginosa	87	56.1
Klebsiella pneumoniae	53	34.1
Streptococcus pneumoniae	7	4.5
Staphylococcus aureus	4	2.6
Escherichia coli (E.coli)	3	1.9
Haemophilus influenzae	1	0.6

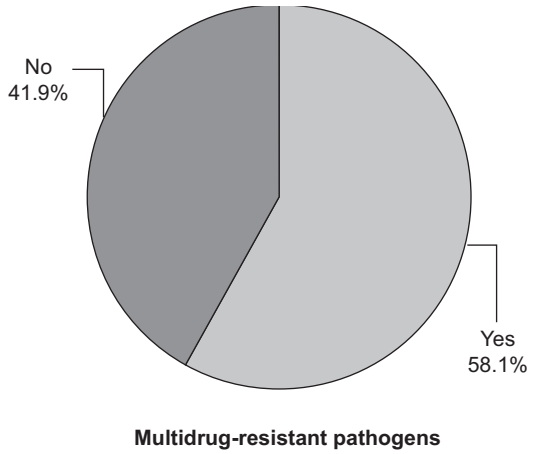

Fig.-2: *Distribution of Multidrug-resistant Pathogens of the Study Cases (n=155)*

Table-III

Distribution of the Study Cases According to Risk Factors for Antibiotic Resistance (n=202)

Risk factors	Number of patients	Percentage
Previous exacerbation	178	88.1
Frequent antibiotic use	122	60.4
Recent hospitalization	103	51.0
Previous use of I/V antibiotics	87	43.1
Previous resistant organisms	30	14.9
Previous ICU admission	16	7.9
Use of immunosuppressive drugs	6	3.0

Table IX shows previous exacerbation 86(95.6%), recent hospitalization 63(70.0%), frequent antibiotic use 69(76.7%), previous I/V antibiotic user 49(54.4%), previous resistant organisms 21(23.3%), diabetes mellitus 56(62.2%) and chronic kidney disease 27(30.0%) in multi-drug resistance, which were statistically significant ($p<0.05$) when compared between multidrug-resistant and non-multidrug resistant pathogen

In univariate analysis, previous exacerbation, recent hospitalization, frequent antibiotic use, diabetes mellitus and chronic kidney disease were found to be independent predictors for MDR pathogens

In multivariate analysis, recent hospitalization, frequent antibiotic use and chronic kidney disease were found to be independent predictors for multidrug resistant pathogens.

Table-IV

Association between MDR Pathogens with Risk Factors (n=155)

Risk factors	Multidrug-resistant pathogens				P value
	Yes (n=90)		No (n=65)		
	n	%	n	%	
Previous exacerbation	86	95.6	54	83.1	0.010[s]
Recent hospitalization	63	70.0	25	38.5	0.001[s]
Frequent use of antibiotics	69	76.7	29	44.6	0.001[s]
Previous I/V antibiotics	49	54.4	26	40.0	0.076[ns]
Previous resistant organisms	21	23.3	7	10.8	0.045[s]
Previous ICU admission	11	12.2	4	6.2	0.207[ns]
Use of immunosuppressive drugs	2	2.2	1	1.5	0.621[ns]
Diabetes mellitus	56	62.2	21	32.3	0.001[s]
Chronic kidney disease	27	30.0	3	4.6	0.001[s]

(s= significant, ns= not significant, p value reached from chi-square test)

Table V

Univariate Regression Analysis for MDR Pathogens (n=90)

	Adjusted OR	95% CI		P value
		Lower	Upper	
Previous exacerbation	4.380	1.327	14.452	0.015[s]
Recent hospitalization	3.733	1.905	7.318	0.001[s]
Frequent antibiotic use	4.079	2.043	8.142	0.001[s]
Diabetes mellitus	3.451	1.762	6.759	0.001[s]
Chronic kidney disease	8.857	2.555	30.707	0.001[s]

(s= significant, *p* value reached from univariate analysis by binary logistic regression analysis, OR= Odds Ratio)

Table-VI

Multivariate Regression Analysis for MDR Pathogens (n=90)

	Adjusted OR	95% CI		P value
		Lower	Upper	
Age (>60 years)	0.614	0.255	1.477	0.276ns
Male	1.005	0.418	2.412	0.992ns
Rural	0.965	0.296	3.146	0.953ns
Smoker	1.519	0.623	3.701	0.358ns
Previous exacerbation	1.420	0.367	5.503	0.612ns
Recent hospitalization	2.423	1.028	5.711	0.043s
Frequent antibiotic use	2.650	1.209	5.808	0.015s
Diabetes mellitus	1.649	0.732	3.715	0.227ns
Chronic kidney disease	5.988	1.572	22.806	0.009s

(s= significant, ns= not significant, *p* value reached from multivariate analysis by binary logistic regression analysis, OR=Odds Ratio)

Discussion:

This cross sectional observational and analytical study was carried out with the aim to identify the possible risk factors for the development of multidrug resistant pathogens. In this study, the age of the patients ranged from 19 years to 83 years with a mean of 47.2±16.3 years. While the mean age was 58.44 and 48 years found in another studies.[9,10,11]

This study observed that a significant number of patients (45.5%) had diabetes mellitus and 16.4% cases had chronic kidney disease. A study[12] showed MDR exacerbations occurred in elderly patients with a higher proportion of comorbid conditions. Diabetes mellitus was found in 7(21.9%) cases among total 32 MDR isolates and chronic renal disease was in 7(21.9%) cases.

This study also explored that majority of the patients had previous exacerbation 178(88.1%).Recent hospitalization was 103(51.0%), frequent antibiotic user was 122(60.4%), previous I/V antibiotic users 87(43.1%), previous ICU admission 16 (7.9%) and previous resistant organism was 30 (14.9%).These findings are consisted with the study findings[12] during the period of 2011 to 2015 among 233 patients.

This study showed bacterial growth found in significant number of cases 155(76.7%). These results are comparable with previous studies[9,13,14,15] and are not supported by the study[10] where bacteriological isolation was found in 35% of cases.

In this study multidrug-resistance was found in 90 (58.1%) while it was 20.1% in another study.[12]

This study also showed previous exacerbation 86(95.6%), recent hospitalization 63(70.0%), frequent antibiotic use 69(76.7%), previous resistant organism 21(23.3%), diabetes mellitus 56(62.2%) and chronic kidney disease 27(30.0%) were found in multi-drug resistance, which were statistically significant ($p<0.05$) when compared between multidrug-resistant and non multi drug-resistant pathogens. Another study[12] reported that exacerbation in last year was 87.5%, hospitalization in previous year was 81.2%, long term oral antibiotics use was 12.5%, Diabetes mellitus was 21.9%, Renal disease was 21.9 %. Hospitalization in previous year and renal disease was statistically significant ($p<0.05$) between groups.

This study observed that in univariate analysis, previous exacerbation, recent hospitalization, frequent antibiotic use, diabetes mellitus and chronic kidney disease were found to be independent predictors for MDR pathogens. Another study[12] documented MDR pathogens were more frequently encountered in patients with more chronic conditions and in those with higher FACED and BSI scores.

In multivariate analysis, recent hospitalization (Odds ratio (OR)2.42, 95% CI 1.03-5.71), frequent

antibiotic use (OR 2.650, 95% CI 1.21-5.80) and chronic kidney disease (OR 5.98, 95%CI 1.57-22.81) were found to be independent predictors for MDR pathogens. Another similar study[12] found three independent MDR risk factors: chronic renal disease (Odds ratio (OR), 7.60, 95% CI 1.92-30.09), hospitalization in the previous year (OR, 3.88 95% CI 1.37-11.02) and prior multidrug-resistant isolation (OR, 5.58, 95% CI 2.02-15.46).

Prior hospitalization is a fairly widely recognized independent MDR risk factor and specifically for MRSA and for Enterobacteriacea mainly related to exposure to 3rd/4th generation Cephalosporin or broad-spectrum Penicillin.[17,18]

Limitations of the study:

Present study was conducted for a short period of time. Sample was taken purposively, so there may be chance of bias. Pathogen identification relied mainly on conventional microbiological tests and extended antibiogram was not possible to conduct in every patient.

Conclusion:

Multidrug resistant bacteria were found in 90 (58.1%) cases. Recent hospitalization, frequent antibiotic use and chronic kidney disease were seemed to be the risk factor for multidrug resistant bacteria.

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Chest Heart Journal
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ORIGINAL ARTICLE

Diseases Pattern in the Department of Physical Medicine & Rehabilitation in a Tertiary Level Hospital

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Abstract:

This is a retrospective study carried out at the department of Physical Medicine and Rehabilitation in National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka for the period of one year from 1st July, 2019 to 30thJune, 2020. The purpose of the study was to observe the disease pattern and demographic characteristics of patients attending the department of Physical Medicine and Rehabilitation in a tertiary care hospital. Total one thousand three hundred and fifty two (n=1352) patients were studied, of which 938(69%) were male and 414(31%) were female. Maximum patients 329(23.90%) belong to above 60 years of age. Maximum patients 973(72%) were come from outside Dhaka city and most of the studied patients were farmers 392(29%). Largest disease group was COPD 202(14.94%). Regarding disease pattern, 913(67.52%) of patientspulmonary problem and rest 439(32.48%) were non pulmonary problem. Among leading diseases, 202(14.94%) were COPD, 182(13.46%) pulmonary fibrosis, 175(12.94%) bronchiectasis, 107(7.91%) lung abscess, 131(9.69%) postsurgical, 116(8.58%) asthma , 126(9.39%) adhesive capsulitis, 119(8.8%) cervical spondylosis, 116(8.58%) low back pain, 77(5.69%) others.

Key words: *Diseases pattern, physical medicine, tertiary hospital*

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DOI: http://dx.doi.org/10.33316/chab.j.v44i2.2019625

Introduction:

Unlike some medical specialties, rehabilitation medicine is not limited to a single organ system. Attention to the whole person is rehabilitation absolute. The goal of the rehabilitation physician is to restore handicapped people to the fullest possible physical, mental, social, and economic independence. This requires analysis of a diverse aggregate of information. Consequently, the person must be evaluated in relation not only to the disease but also to the way the disease affects and is aûected by the person's family and social environment, vocational responsibilities, economic state, interests, hopes and dreams.[1] The field of Physical Medicine and Rehabilitation focuses on the restoration of health and function and reintegration of the patient into the community.[2,3] Physical Medicine department was established in NIDCH in 1969. Since establishment, department of Physical Medicine is providing services as outdoor basis and referred indoor cases regularly

Physical Medicine & Rehabilitation Department, NIDCH provides services to the patients with respiratory and thoracic problems from the

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beginning. This department tries to correlate with other departments (Respiratory medicine and Thoracic surgery) in providing facilities, faith and satisfaction to the patients. This study was carried out with the intention to provide information about demographic data & disease pattern among the patients receiving treatment in the department of Physical Medicine and Rehabilitation, NIDCH, Dhaka.

Methods:

This is a retrospective review of the records at National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka for the period of one year from 1st July, 2019 to 30thJune, 2020. The subjects were enrolled on an individual basis, despite the varying number of visits by a given patient during the period of study. Data was analyzed using microsoft excel and statistical package for social software (SPSS). Means and standard deviation were used for continuous variables, and simple proportions were used for categorial data.

Results:

Total number of patients was 1352. Among them 938 (69.38%) were male and 414 (30.62%) were female. (Figure -1)

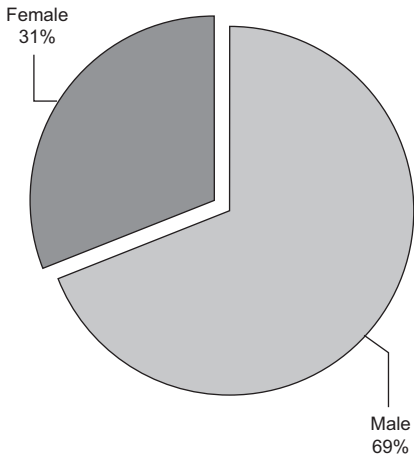

Fig.-1: *Sex distribution of the patients*

4.89% of patients were under 20 years of age, about 71% of patients belong to 2nd, 3rd, 4th, 5th decades. 24.33% were above 60 years of age (Figure -2).

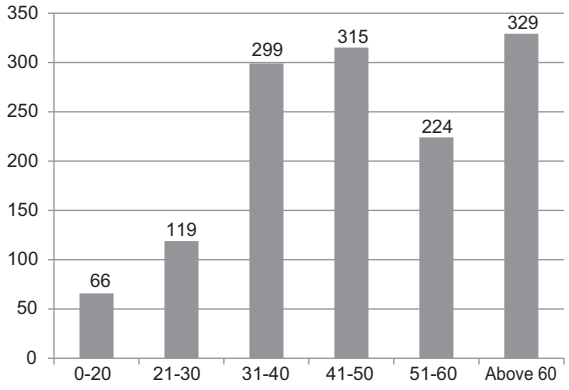

Fig.-2: *Age distribution of the patients*

71.97%of the patients were from outside the Dhaka city. Rest of the patients (28.03%) was from within Dhaka. (Figure -3)

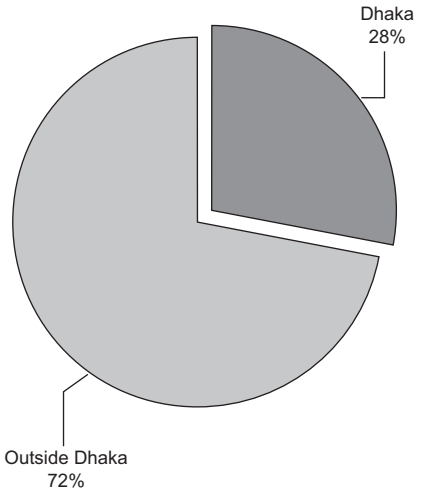

Fig.-3: *Distribution of patients according to catchment area.*

Among the total number of patients, majority(392) were Farmers (28.99%) followed by Housewives (27.29%), Labourer (19.94%), Service holder (10.58%), Businessman (9.32%) and Student(8.87%). (Figure -4)

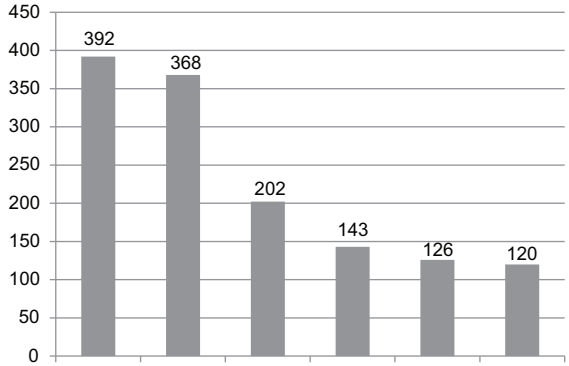

Fig.-4: *Distribution of the patients according to occupation.*

Among 1352 patients, 767 patients (56.74%) were from indoor and 585 patients (43.26%) were from outdoor. (Figure -5)

Regarding disease pattern, 913(67.52%) of patients were pulmonary problems and 439(32.48%) were

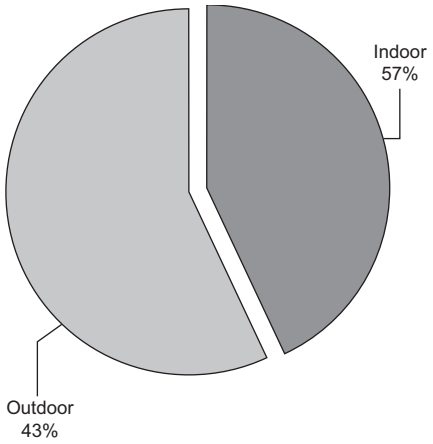

Fig.-5: *Distribution of patients according to inter hospital visit.*

non pulmonary problem.Among leading diseases, 202(14.94%) were COPD, 182(13.46%) pulmonary fibrosis, 175(12.94%) bronchiectasis, 116(8.58%) asthma, 131(9.69%) postsurgical, 107(7.91%) lung abscess 126(9.39%) adhesive capsulitis, 119(8.8%) cervical spondylosis, 116(8.58%) low back pain, 177(5.69%) others.

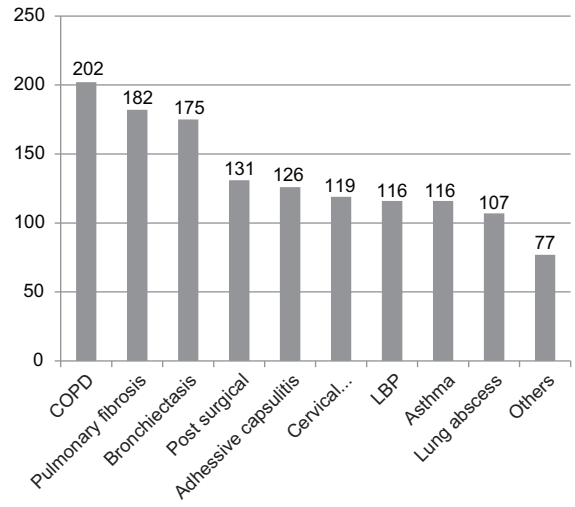

Fig.-6: *Disease proûle of the patients*

Table-I
Leading diseases

Disease	Number of patients	Percentage
COPD	202	14.94%
Pulmonary fibrosis	182	13.46%
Bronchiectasis	175	12.94%
Post-surgical	131	9.69%
Adhesive capsulitis	127	9.39%
Cervical spondylosis	119	8.8%
Low back painAsthma	116	8.58%
Lung abscess	107	7.91%
Others	77	5.69%

Discussion:

In this study it has been tried to ûnd out the age, sex, occupation, residency and disease pattern of the patients attending the dept. of Physical Medicine & Rehabilitation, NIDCH. In this study, 69.38% of patients were male and 30.62% were female. A retrospective study at tertiary level hospital for disease pattern in the department of physical medicine and rehabilitation by Hossain MS et al showed that 52% were female and 42% were male.[4]

A cross sectional study at community level for detection of painful musculoskeletal disorders by Moinuddin M et al showed that musculoskeletal complaints are predominant in females[5] Moniruzzaman M in RpMCH showed 55.1% werefemale patients.[6] In this study male are more due to more exposure.

Occupation of patients was farmers (28.99%), Houseives (27.29), labourer (19.94%), serviceman (10.58%), businessman (9.32%), &student (8.87%).Hossain MS et al found housewives (36.73%), farmer (15.56%), service holder (13.35%) in their study.

MoinuddinM et al5 found housewives were 52.33% and Nessa J et al were 37.3% housewife, 16.3% farmer,15.1% service holder in their studies.[6]

4.89% of patients were under 20 years of age, 8.8% were 21-30 years, 22.12% were 31-40 years, 23.30% were 41-50 years, 16.58% were 51-60 years and 24.33% were above 60 years of age. Hossain MS et al showed most (27.96%) were between 41-50 years. MoinuddinM et al. showed most (23.36%) were between 40-49 years, MoniruzzamanM et al.[7] also found 49.9% were in 41-50 years age.

In this study majority of patients had COPD-14.94%, Pulmonary fibrosis-13.46%, bronchiectasis -12.94, asthma-8.58%, post surgical-9.69% & shoulder pain-9.39%. Hossain et al showed that majority of patients (16.77%) had non specific low back pain.Moinuddin M et al showed that majority of patients (44.85%) had back pain.[5] Study performed by Rahman MM et al at CMCH,[8] Nessa J et al at ShaheedSuhrawardy MCH[7] and Moniruzzaman M at RpMCH6 found highest level of back pain in their study respectively. Hasan SA et al documented non-speciûc low back pain (59.95%) as most common disease in his study.[9,10,11]

In National institute of diseases of the Chest & Hospital the referral system & interaction among different departments is improving gradually and importance of Physical medicine & rehabilitation department is being appreciated. This may be one of the reason for increasing is pulmonary rehabilitation has great role in increasing the quality of life of the patients suffering from pulmonary problems. From the above discussion, it is clearly demonstrated that the ûndings of the study performed in Physical Medicine department of NIDCH is consistent with the ûndings of different institutes of Bangladesh.

The total numbers of patients attending Physical Medicine Department have been increasing day by day. Most of the patients coming to this department from outside the Dhaka city. This study is done in one tertiary level hospital of Bangladesh in a small population and it may not reûect the total scenario of patients getting treatment from Physical Medicine & Rehabilitation department.

A uniform data system (UDS) for Medical Rehabilitation is maintained in USA and published annually. No such system exists in Bangladesh. A large scale multi-centered study should be performed in the country. A uniform data system should be constructed for Medical rehabilitation in Bangladesh.

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REVIEW ARTICLE

Cardiopulmonary Exercise Test: Applications and Interpretation

Pulak Kumar Dey[1], Mita Bhowmik[2], Sanjoy Kumar Kar[3] , Subrata Kumar Gain[3]

Abstract:

Cardiopulmonary exercise test (CPET) is often an overlooked and underutilized modality but offers an ocean of information about a patient's functional status. The following parameters are measured: ventilation; oxygen consumption (VO2); carbon dioxide production (VCO2); and the other variables of conventional exercise testing. The CPET allows defining mechanisms related to low functional capacity that can cause symptoms, such as dyspnoea, and correlate them with changes in the cardiovascular, pulmonary and skeletal muscle systems. Indications include evaluation of dyspnea, distinguishing cardiac vs pulmonary vs peripheral limitation vs others and detection of exercise-induced bronchoconstriction.

Exercise modalities are cycle ergometer and treadmill. In heart disease breathing reserve is >30%, and heart rate reserve is <15%, in pulmonary disease breathing reserve is <30% but heart rate reserve is >15%.

Key words: *Exercise Test; Oxygen Consumption; Carbon dioxide production; Anaerobic threshold, Breathing resrve; Heart rate reserve.*

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Introduction:

Cardiopulmonary exercise test (CPET) is often an overlooked and underutilized modality but offers an ocean of information about a patient's functional status. In its most frequent applications, CPET consists in applying a gradually increasing intensity exercise until exhaustion or until the appearance of limiting symptoms and/or signs. The following parameters are measured: ventilation; oxygen consumption (VO2); carbon dioxide production (VCO2); and the other variables of conventional exercise testing. The CPET provides joint data analysis that allows complete assessment of the cardiovascular, respiratory, muscular and metabolic systems during exertion, being considered gold standard for cardiorespiratory functional assessment.[1-6]

The CPET allows defining mechanisms related to low functional capacity that can cause symptoms, such as dyspnoea, and correlate them with changes in the cardiovascular, pulmonary and skeletal muscle systems. Furthermore, it can be used to provide the prognostic assessment of patients with heart or lung diseases, and in the preoperative period, in addition to aiding in a more careful exercise prescription to healthy subjects, athletes and patients with heart or lung diseases.

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Indications[7]:

1. Evaluation of dyspnea	6. Preoperative evaluation and risk stratification
2. Distinguish cardiac vs pulmonary vs peripheral limitation vs others	7. Prognostication of life expectancy
3. Detection of exercise-induced bronchoconstriction.	8. Disability determination
4. Detection of exertional desaturation.	9. Fitness evaluation
5. Chest physiotherapy: Exercise intensity/ prescription, response to participation	10. Confirms diagnosis
	11. Assess response to therapy

Contraindication[7]

Absolute Contraindica	Relative Contraindication
Acute myocardial infarction	Left main or 3-V CAD
Unstable angina	Severe arterial HTN (>200/120)
Unstable arrhythmia	Significant pulmonary HTN
Acute endocarditis, myocarditis, pericarditis	Tachyarrhythmia, bradyarrhythmia
Syncope.	High degree AV block
Severe, symptomatic atrial stenosis	Hypertrophic cardiomyopathy
Uncontrolled CHF	Electrolyte abnormality
	Moderate stenotic valvular heart disease
	Advanced or complicated pregnancy
	Orthopedic impairment

Procedure:

Initial assessment

- **History:** Regarding tobacco use, medications, tolerance to normal physical activities, any distress symptoms, contraindicated illnesses
- **Physical Exam:** Height, weight, assessment of heart, lungs, peripheral pulses, blood pressure
- **ECG**
- **Pulmonary Function Tests:** spirometry, lung volumes, diffusing capacity, arterial blood gases

Prior To Test

Should wear loose fitting clothes, low-heeled or athletic shoes ,should be abstain from coffee and cigarettes at least 2 hours before the test, maintenance of medications, may eat a light meal at least 2 hours before the test.

Exercise modalities: cycle ergometer and treadmill

Advantages of cycle ergometer :

Cheaper, safer, less danger of fall/injury, can stop anytime, direct power calculation, independent of weight, holding bars has no effect, little training needed, easier BP recording, requires less space, less noise

Advantages of treadmill:

Attains higher VO2, more functional

Indication of test termination[7]

Patient's request: fatigue, dyspnea, pain, ischemic ECG changes (2 mm ST depression), chest pain suggestive of ischemia, significant ectopy,2nd or 3rd degree heart block, systolic BP >0-250, diastolic BP>110-120,fall in BP sys>20 mmHg, SpO2<81-

85%, dizziness, faintness, onset of confusion, onset of pallor

General Mechanisms of Exercise Limitation:

1) Pulmonary

Ventilatory impairment, respiratory muscle dysfunction, impaired gas exchange

2)Cardiovascular

Reduced stroke volume, abnormal HR response, circulatory abnormality, blood abnormality

3)Peripheral

Inactivity, atrophy, neuromuscular dysfunction,

reduced oxidative capacity of skeletal muscle, malnutrition, perceptual, motivational, environmental

CPET Measurements:

- Work, VO2, VCO2, AT, HR, ECG, BP,RR, SpO2,ABG,Lactate,dyspnea, leg fatigue

Pulmonary Parameters

1. Minute Ventilation
   - Normal = 5 –6 liters/ min. At Exercise = 100 liters/min. Increase is due to stimulation of the respiratory centers by brain motor cortex, joint propioceptors and chemoreceptors.
2. Breathing Rate
   - Normal = 12 –16 / min, At Exercise = 40 –50 / min, responsible for the increase in minute ventilation. In Anaerobic Threshold (AT) the minute ventilation increases more than the workload
3. Tidal Volume
   - Normal = 500 ml, During Exercise = 2.3 –3 liters.
4. Dead Space / Tidal Volume Ratio
   - Normal = 0.20 –0.40. At Exercise =0.04 – 0.20. Decrease is due to increased tidal volume with constant dead space
5. Pulmonary Capillary Blood Transit Time
   - Normal = 0.75 second. At Exercise =0.38 second. The decrease is due to increased cardiac output
6. Alveolar-Arterial Oxygen Difference
   - Normal =10 mm Hg. At Exercise = 20 –30 mm Hg, changes very little until a heavy workload is achieved
7. Oxygen Transport

   Increase in temperature, PCO2 and relative acidosis in the muscles, increase in release of Oxygen by blood for use by the tissues for metabolism
8. Pulmonary ventilation (VE): expressed as liters per minute, is the volume of air moved in and out of the lungs. It is determined as the product of respiratory rate by the volume of air exhaled at every cycle (tidal volume). At rest, 7 to 9 L/min are ventilated, but in athletes that value can reach 200 L/min at maximal exertion.6It reflects disease severity and relates to worse prognosis in patients with HF.3-5

9) Breathing Reserve (VE/MVV): represents the ratio between maximal ventilation during exercise (VE) and maximum voluntary ventilation (MVV) at rest, both variables in L/ min. It is useful in the differential diagnosis of dyspnea related to pulmonary mechanism.6

Cardiovascular Parameters

1. Cardiac Output
   - Normal =4 –6 liters / min. At Exercise = 20 liters / min, increase is linear with increase in workload during exercise until the point of exhaustion. In first half of exercise capacity, the increase is due to increase in Heart Rate and Stroke Volume, later due to increase in Heart Rate alone.
2. Stroke Volume
   - Normal = 50 –80 ml. At Exercise : double

     increase is linear with increase in workload but after a Heart Rate of > 120/ min, there is little increase in Stroke Volume
3. Heart Rate
   - Normal =60 –100 /min. At Exercise = 2.5 –4 times the resting HR. HR max is achieved just prior to total exhaustion, physiologic endpoint of an individual. HR max = 220 – age or HR max = 210 –(0.65 x age)

Heart Rate Reserve

Comparison of actual peak HR and predicted peak HR

= (1 –Actual/Predicted) x100%

Normally <15%

4. Blood Pressure

   During Exercise:

   • Systolic BP increases (to 200 mm Hg). Diastolic BP is relatively stable (up to 90 mmHg). Increase in Pulse Pressure (difference between Systolic and Diastolic pressures) .

Metabolic Parameters

1) Oxygen Consumption:

   $Vo_2 = (SV \times HR) \times (Cao_2 - Cvo_2)$

   Normally 250 ml / min. 3.5 –4 ml / min / kg increases directly with the level of muscular work and increases until exhaustion occurs .

   VO2max = maximum level of oxygen consumption anddefinite indicator of muscular work capacity.

   Normal Range is 1,700 –5,800 ml / min

   The term 'peak VO2' is used as a synonym for VO2 max throughout this text. Peak VO2 is considered abnormal when below 85% of the predicted value.[6] It has been used as a universal marker1-3,5

2). Carbon Dioxide Production

   • Normally 200 ml / min. 2.8ml / min / kg. At Exercise,

   In initial phase, increases at same rate as VO2, Once Anaerobic Threshold (AT) is reached, increases at a faster rate than VO2

3) Lactate threshold (θL)[8]
   Lactic Acid is Buffered by Bicarbonate
   Lactic acid + HCO3→H2CO3+ Lactate
   ↓
   H2O + CO2

   θL is the highest $v´O_2$ at which arterial lactate is not systematically increased, and is estimated using an incremental test. It is considered an important demarcator of exercise intensity. Noninvasive estimation of θL requires the demonstration of an augmented $v´cO_2$ in excess of that produced by aerobic metabolism , and its associated ventilator sequel.

4) Anaerobic Thershold (At)

   • Normal: occurs at about 60% of VO2 max followed by breathlessness, burning sensation begins in working muscles increase is due to increased acid production

   The normal mean AT values expected for adults are around 40% to 65% of peak VO2.6 The AT values are important for the individualized prescription of exercise, as well as for the diagnosis of anemia, physical unfitness, myopathies and cardiopathies in the presence of values lower than the predicted ones.[2-6]

5) Respiratory Quotient (RQ)
   RER = CO_2produced / O_2consumed
   = VCO2/ VO2

   • Resting Level = 0.8

   Values above 1.0 can reflect intense exercise, but those ee 1.10 are those searched on CPET, and have been accepted as a parameter of exhaustion or quasi-exhaustion.3,7

6) Blood PH
   relatively unchanged until AT is reached, the body becomes less able to buffer the excessive acid produced by anaerobic metabolism

7) Arterial –Venous Oxygen Content Difference ($Cao_2 - Cvo_2$)

   • mLof O2 / 100 ml of blood. Normal = 5 vol%. At Exercise = 2.5 –3 times higher

8) Ventilatory Equivalents

   Ventilatory equivalent for carbon dioxide = Minute ventilation / VCO2

   Efficiency of ventilation, Liters of ventilation to eliminate 1 L of CO2

   Ventilatory equivalent for oxygen = Minute ventilation / VO2

   • Liters of ventilation per L of oxygen uptake

   Relationship of AT to RER and Ventilatory Equiv for O2

   • Below the anaerobic threshold, with carbohydrate metabolism, RER=1 (CO2production = O2consumption).
   • Above the anaerobic threshold, lactic acid is generated.
   • Lactic acid is buffered by bicarbonate to produce lactate, water, and carbon dioxide.
   • Above the anaerobic threshold, RER >1 (CO2production > O2consumption).
   • Carbon dioxide regulates ventilation.
   • Ventilation will disproportionately increase at lactate threshold to eliminate excess CO2.

Increase in ventilator equivalent for oxygen demarcates the anaerobic threshold.

Patients with inadequate ratio between pulmonary ventilation and pulmonary perfusion (increased physiological dead space) ventilate inefficiently and have high VE/VO2 values (pulmonary disease and HF).6 Peak values above 50 have been useful to diagnose patients suspected of having mitochondrial myopathy.10 On the other hand, VE/VCO2 represents the ventilatory need to eliminate a certain amount of CO2 produced by active tissues, being influenced by partial pressure of carbon dioxide (PaCO2). The VE/VCO2 slope reflects the severity and prognosis of patients with HF, pulmonary hypertension, HCM, COPD and restrictive pulmonary disease.1,3-5,8,11,12

8)End-tidal CO2 partial pressure (PETCO2): reflects ventilation–perfusion within the pulmonary system, and, indirectly, cardiac function.6 Its value ranges from 36 to 42 mmHg, with 3- to 8-mmHg elevations during moderate intensity exercise, reaching a maximal value with subsequent drop, due to VE increase, characterizing RCP.1

9)△VO2/△WR Relationship: relationship between VO2 (Y axis in mL.min-1) and workload (X axis in Watts), measured only during exercise on a cycle ergometer with ramp protocol, whose value is progressively and linearly incremented until maximal effort. It is useful in the diagnosis of patients suspected of having myocardial ischemia with left ventricular dysfunction on exertion. Its normal value for adults is 9 mL.min-1.W-1 (the lowest limit being 8.6 mL.min-1.W-1).

Interpretation of CPET[7]

- Peak oxygen consumption
- Peak HR
- Peak work
- Peak ventilation

Estimation of Predicted Peak HR

Which is =220 –age

- For age 40 : 220 -40 = 180
- For age 70 : 220 -70 = 150

Or 210 –(age x0.65)

- For age 40: 210 -(40 x0.65) = 184
- For age 70: 210 -(70 x0.65) = 164

Heart Rate Reserve

Comparison of actual peak HR and predicted peak HR

= (1 –Actual/Predicted) x100%

Normally <15%

Oxygen Pulse

O2 PULSE = VO2/ HR

Normally 2.5 –4 ml O2 / heartbeat. At Exercise = 10 –15 ml

With increasing muscle work during exercise, each heart contraction must deliver a greater quantity of oxygen out to the body

Under certain circumstances, the morphological analysis of its curve aids in the diagnosis of ventricular dysfunction and important effort-induced myocardial ischemia.1,3-6

Increases During Exercise[7]

Heart rate, Oxygen extraction, cardiac output, oxygen uptake, carbon dioxide out, minute ventilation, alveolar ventilation, oxygen pulse, RQ and RER,METS , arterial blood pressure

DECREASES DURING EXERCISE[7]

During exercise, there are decreases in: VD/ VT

Comparison CPET results[7]

	Normal	CHF	COPD
Predicted Peak HR	150	150	150
Peak HR	150	140	120
MVV	100	100	50
Peak VO_2	2.oo	1.2	1.2
AT	1.oo	0.6	1.0
Peak VE	60	40	49
Breathing Reserve	40%	60%	2%
HR Reserve	0%	7%	20%
Borg Breathlessness	5	4	8
Borg leg discomfort	8	8	5

CPET Interpretation[7]

	Peak VO_2	HRR	BR	AT/$VO_{2\ max}$	A-a
Normal	>80%	<15%	>30%	>40%	normal
Heart Disease	<80%	<15%	>30%	<40%	normal
Pulmonary vascular disease	<80%	<15%	>30%	<40%	increased
Pulmonary mechanical disease	<80%	>15%	<30%	>40%	increased
Deconditioning	<80%	>15%	>30%	>40%	normal

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CASE REPORT

A Young Man with Dieulafoy,s Lesion in Proximal Stomach - A Uncommon Case Report

M. Rahman Mia[1], M. Anamul Hoque[2], N. Islam[3]

Abstract :

Dieulafoy's lesions are a rare but challenging cause of upper GI bleeding due to their intermittent nature. This lesions contribute approximately 6% of non-variceal upper GI bleeds and 1-2% of all GI bleeding. This quiescent lesions are easily overlooked on endoscopy and the bleeding lesions are occationally misidentified. Increased awareness and advances in the endoscopic techniques are important for accurate diagnosis.

A case of 32 years young man present with Dieulafoy,s lesion in proximal stomach has been described here.

Keywords : *Dieulafoy,s, stomach, meleana, gastrectomy*

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Introduction:

Dieulafoy lesion (DL) in the gastrointestinal (GI) tract is a rare but important cause of GI bleeding; massive bleeding from this lesion can be fatal unless adequate treatment is promptly initiated.[1] In approximately 4-9% massive upper gastrointestinal haemorrhage, no demonstrable cause can be found.[2] Dieulafoy's lesion is thought to be the cause of acute and chronic upper gastrointestinal bleeding in approximately 1-2% of these cases .[3] The incidence, however, might vary from 0.5% to 14%. It is thought to be more common in males (M:F = 2:1) with a median age of 54 years at presentation. There is usually no significant NSAIDs or alcohol abuse.[4] Although the exact cause is not known, pathogenesis of this condition is considered to be the presence of abnormal large-caliber arteries at the submucosal level, subsequently causing the thinning of the overlying mucosa, producing erosions and leading to exposure of the vessel wall to the lumen, finally with the possibility of developing digestive hemorrhage.[5]

We describe a uncommon case report, a 32 years young man had dieulafoy lesion in fundus & proximal body of stomach presented with meleana underwent sub-total gastrectomy by left thoraco-abdominal incision.

Case Report:

Mr. Rathindranath 32 years young man garment,s worker came from Shripur, Magura presented with passage of black colour stool, abdominal fullness and severe weakness. His presenting symptoms started from about 12 years back. Initially he had H/O occationally passage of black stool and red coloured stool alternately as interval of 2-3 months and persist for 3-4 days. Gradually that was increased

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and passaged black stool frequently. He also noticed occational central abdominal pain which was colicky in nature, persist few hours, no radiation and relieved after defaecation. He also felt abdominal fullness and nausea but no vomiting. Gradually he developed very weakness and unable to performed daily activities. For that, around on 2009 he treated in Kolkata,india 2 times and investigated, took medication and h/o blood transfusion 2 bags. But his problem not improved and again he treated in Chennai, India on 2016 and lastly on 2020 and diagnosed as dieulafoy,s lesion in stomach. His bladder habit was normal. No h/o cough, heamoptysis, chest pain, heamatemesis, jaundice, bone pain or headache. For definitive treatement, he was admitted in our unit in NIDCH on 05/01/21 (reg.- 95/22) .

He had no co-morbidities. He had no past medical or surgical history but h/o taking blood transfusion several times. No significant family history. No allery to any specific food or medicine. He was non-smocker and non-alcoholic.he was married and father of one son. He came from low class family and was immunized according EPI schedule. On physical examination, we found patient looked weak and anxious. Found severely anaemic but not ecteric and mildly dehydrated. All other vitals were normal limit, had no any peripheral lymphadenopathy including neck gland. Abdomen, Chest and other systemic examination revealed normal findings.

CXR-P/A view and CT abdomen found normal findings. Upper GI endoscopy found Dieulafoy,s lesion in fundus of stomach.

TC 99m leveled RBC scanning revealed active bleeding site found in fundus and proximal body of stomach.

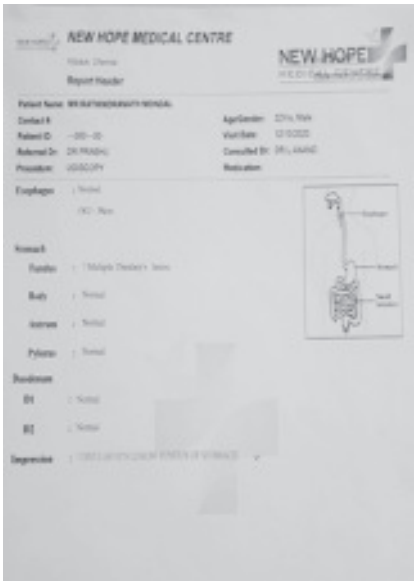
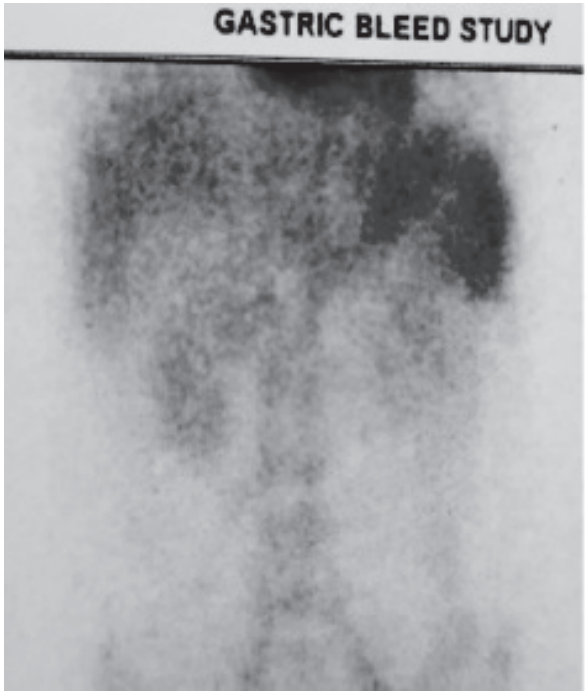
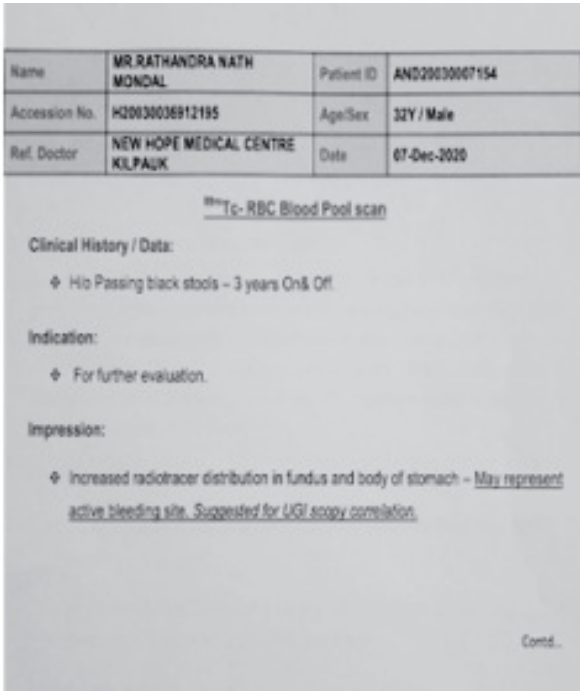


Fig.-1: *Upper GI endoscopy*

All other routine investigations found within normal limit but only Hb% was very low level (4.1 g/dl).





Name	MR.RATHANDRA NATH MONDAL	Patient ID	AND20030007154
Accession No.	H20030036912195	Age/Sex	32Y / Male
Ref. Doctor	NEW HOPE MEDICAL CENTRE KILPAUK	Date	07-Dec-2020

^{99m}Tc- RBC Blood Pool scan

Clinical History / Data:

- H/o Passing black stools – 3 years On& Off.

Indication:

- For further evaluation.

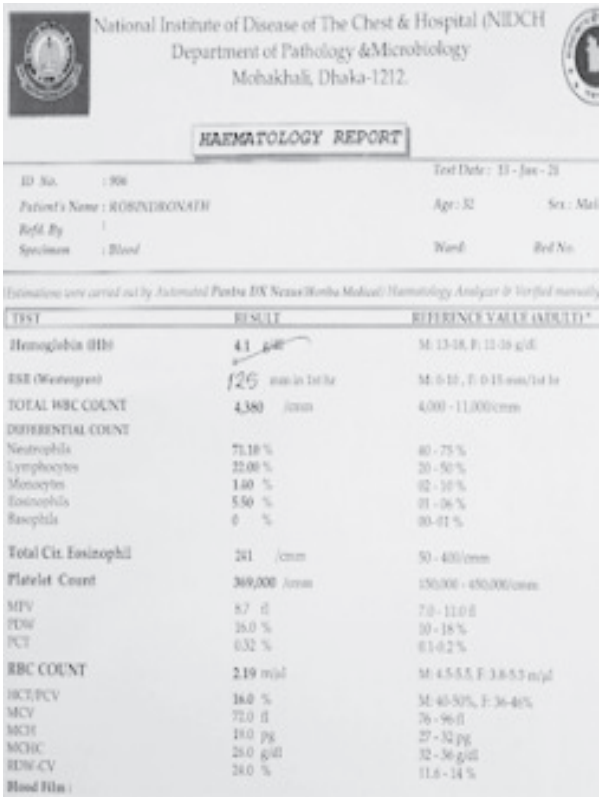
Impression:

- Increased radiotracer distribution in fundus and body of stomach – May represent active bleeding site. Suggested for UGI scopy correlation.

Contd..

Fig.-2: *TC leved RBC scaning*

So we planned for sub-total or total gastrectomy through Left thoraco-abdominal incision Under G/A with one lung ventilation. Patient underwent thorough pre anesthetic check up and pre-operative optimization was done, then surgery was performed. During procedure, diaphragm was cut along the incision line and there was no collection within abdominal & thoracic cavaity, liver and other organ found normal. Proximal stomach found congested and huge omental fat & adhesions were visualized. Stomach was mobelised by ligasure and bipolar diathermy from distal esophagus to first part of duodenum and preserved blood circulation specially in distal stomach. Then excised from gastro-esophageal junction to distal part of body of stomach preserved only pylorus and anastomosis done between distal esophagus & pyloric part of stomach used linear and circular steplers. Total specimen, part of distal esophagus and distal stomach sent for histopathology separately. Then checked any injury/ leak of anastosis and a NG tube kept distal to anastomosis. Then diaphragm closed by two layers. Also saw lung expansion properly.



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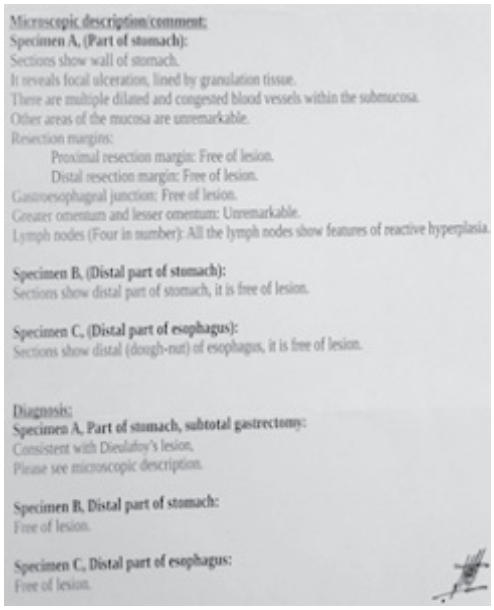
HAEMATOLOGY REPORT

TEST	RESULT	REFERENCE VALUE (ADULT)
Hemoglobin (Hb)	4.1	M: 13-18, F: 11-16 g/dl
ESR (Westergren)	125	M: 0-10 , F: 0-15 mm/1st hr
TOTAL WBC COUNT	4,380	4,000 - 11,000/cmm
DIFFERENTIAL COUNT		
Neutrophils	71.10 %	40 - 75 %
Lymphocytes	22.00 %	20 - 50 %
Monocytes	1.60 %	02 - 10 %
Eosinophils	5.50 %	01 - 06 %
Basophils	0 %	00-01 %
Total Cit. Eosinophil	241 /cmm	50 - 400/cmm
Platelet Count	369,000	150,000 - 450,000/cmm
MPV	8.7 fl	7.0 - 11.0 fl
PDW	16.0 %	10 - 18 %
PCT	0.32 %	0.1-0.2 %
RBC COUNT	2.19 m/cl	M: 4.5-5.5, F: 3.8-5.5 m/µl
HCT/PCV	16.0 %	M: 40-50%, F: 36-46%
MCV	72.0 fl	76 - 96 fl
MCH	19.0 pg	27 - 32 pg
MCHC	26.0 g/dl	32 - 36 g/dl
RDW-CV	28.0 %	11.6 - 14 %
Blood Film :		

Fig.-3: *Hematological report*

After sequired haemostsis,a chest drain kept in situ and wound closed in layers. Dieulafoy,s lesion was confirmed histopathologically in our case and proximal & distal margine free of lesion.

Post operative recovery was uneventful. On 7th POD contrast X-ray of oesophagus & stomach done which revealed no leak. Also gave orally Xension violet mixed water to checked any leak. On 8th POD NG tube removed and gave liquid diet. On 9th POD chest drain removed. All skin clips were removed on 12th POD and then discharged with advice.



Microscopic description/comment:
Specimen A, (Part of stomach):
Sections show wall of stomach.
It reveals focal ulceration, lined by granulation tissue.
There are multiple dilated and congested blood vessels within the submucosa.
Other areas of the mucosa are unremarkable.
Resection margins:
Proximal resection margin: Free of lesion.
Distal resection margin: Free of lesion.
Gastroesophageal junction: Free of lesion.
Greater omentum and lesser omentum: Unremarkable.
Lymph nodes (Four in number): All the lymph nodes show features of reactive hyperplasia.

Specimen B, (Distal part of stomach):
Sections show distal part of stomach, it is free of lesion.

Specimen C, (Distal part of esophagus):
Sections show distal (dough-nut) of esophagus, it is free of lesion.

Diagnosis:
Specimen A, Part of stomach, subtotal gastrectomy:
Consistent with Dieulafoy's lesion.
Please see microscopic description.

Specimen B, Distal part of stomach:
Free of lesion.

Specimen C, Distal part of esophagus:
Free of lesion.

Fig.-4: *Microscopic description of specimen.*

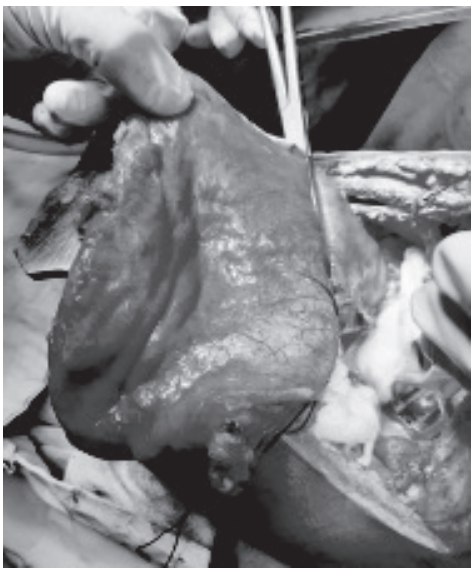


Fig.-5: *after mobilization stomach*

Fig.-6: *after excision of stomach*

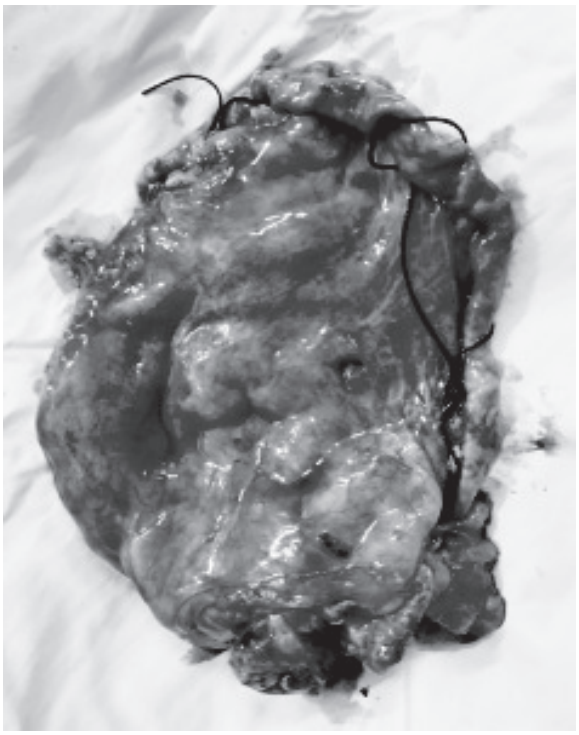


Fig.-7: *Excised specimen*

Fig.-8: *specimen (mucosa)*

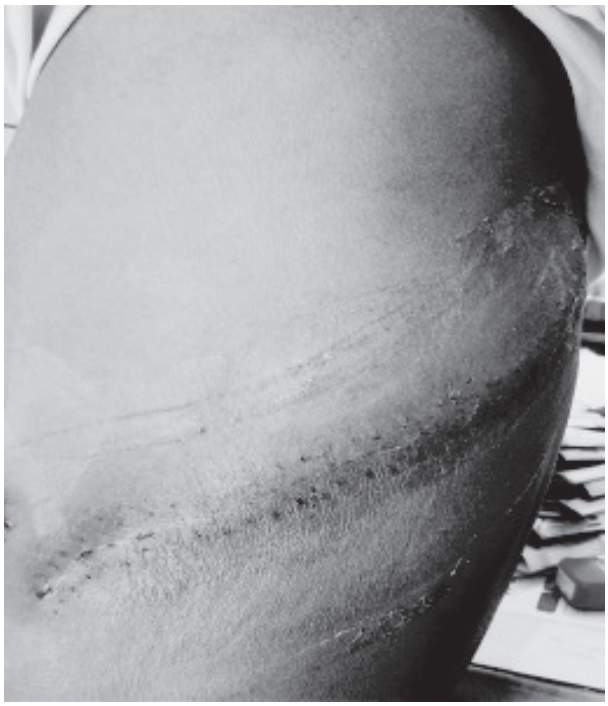


Fig.-9: *post.operative wound*

Discussion:

Dlafoy,s lesion is one of the rare causes of GI bleeding. It accounts for about 1.5% of all GI hemorrhages.[6]

It is caused by an abnormally large calibre persistent tortuous submucosal artery. This has been demonstrated by histological examination of resected specimens. The artery protrudes through

a solitary, tiny mucosal defect (2-5 mm), commonly in the upper part of the stomach. It may rupture spontaneously and lead to massive bleeding. It has been suggested that the thin mucosa overlying a pulsating artery is eroded progressively by the mechanical pressure from the abnormal vessel.[7] This lesion was first described by Gallard and later named for the French surgeon Georges Dieulafoy who called it "exulceratio simplex" believing that it was the first stage of a gastric ulcer, the progression of which being stopped by the occurrence of hemorrhage.

The majority of DL occur in the proximal stomach, typically located within 6 cm of the gastroesophageal junction on the lesser curvature, due to arterial vessels directly branching from the left gastric artery[8] but they have also been reported in the esophagus, small and large bowel and also other rare locations such as the rectum or the gallbladder and even in extra-GIT like bronchus.[9]

The cause is unknown. In contrast to peptic ulcer disease, a history of alcohol abuse or NSAID use is usually absent in Dieulafoy's lesion.The most common presenting symptom is recurrent, often massive, haematemesis associated with melaena (51%). The lesion may present with haematemesis alone (28%), or melaena alone (18%). Our patient presented with mainly melaena. Characteristically, there are no symptoms of dyspepsia, anorexia or abdominal pain. Initial examination may reveal haemodynamic instability, postural hypotension and anaemia. A Dieulafoy's lesion is difficult to diagnose, because of the intermittent pattern of bleeding. Endoscopy reveals a reddish-brown protruding spot with small erosion and no ulcer. DL is more easily identified when pulsating or oozing blood. Elective endosonography to examine spots suspected to be DLs is helpful in confirming the diagnosis.[10] In difficult cases, angiography & TC 99m leveled RBC scaning may be useful when endoscopy fails to identify the lesion.

Traditionally, the treatment of DL was surgical. However, with the development of endoscopic haemostasis techniques, the need for surgery has been reduced, and the mortality rates have decreased from 80% to 8.6%. Therefore, the current treatment of choice in accessible lesions is endoscopy, with a success rate of > 90% and low rates of recurrence and complications. The endoscopic haemostasis procedures are classified into three groups: (1) thermal: electrocoagulation, heater probe and argon plasma coagulation (2) local injection of substances, such as adrenaline or sclerosing solutions; and (3) mechanical: haemostatic clips and bands. However, in the clinical field, the choice of a procedure depends on the experience, decision of the endoscopist and the field of vision.[11] Surgical procedures currently employed include under-running of the lesion or a wedge resection of the affected section of gut. Angiography may also be used therapeutically by gelfoam embolisation. This type of treatment is usually reserved for patients who are not amenable to endoscopic therapy and are poor surgical candidates.

Our patient had Dieulafoy,s lesion in fundus & proximal part of body of stomach and done sub-total gastrectomy by left thoraco-abdominal incision successfully with symptomatic improvement of the patient.

Conclusion:

Although uncommon, Dieulafoy's lesions should always be considered as a differential in any patient with massive painless GI bleeding. Due to its intermittent nature, initial evaluation may not identify the lesions thus requiring repeat exams and they are associated with a high rate of re-bleeding.Though surgical excision decrease the chance of re-bleeding, various endoscopic methods are the modality of choice for the identification and treatment of gastric Dieulafoy's lesions now a day. A hope of this case report is to encourage providers to remember this potential cause and to facilitate its management when dealing with such dilemmas of chronic anemia, gastrointestinal bleeding, and ongoing hematemesis, meleana.

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CASE REPORT

Management of "O" Positive Patient, Transfused with "B" Positive Blood – A Case Report

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Abstract:

The complications of blood transfusion are well known and at times is life threatening especially when it occurs due to accidental major mismatched blood transfusion. Here we present a case of a 32 years old lady who delivered a baby by LUCS. On her 3rd POD, she came to a tertiary level hospital with profuse per vaginal bleeding, breathlessness. She received an erroneous transfusion of group "B" Rh positive blood when her actual blood group was "O" Rh positive at a different hospital. She presented with features of DIC and acute renal failure. She was admitted to critical care unit- treated with broad spectrum antibiotics, forced diuresis with inj. Frusemide and eventually 3 sessions of hemodialysis were needed. As for transfusion, we decided to transfuse her with "O" Rh positive washed packed cell and "AB" Rh positive plasma which finally saved her life.

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Introduction:

The ABO and Rh blood group system is the most important system which is followed prior to all blood transfusion.[1] Rhesus Blood Group system is the second most important blood group system followed during blood transfusion.[2] Blood group "O" is the commonest which is 37.12% of the world population, this is followed by "B" at 32.26%. "A" group comprises of 22.88% of the people and "AB" is the least prevalent group at only 7.74%. Similarly, out of the total donor population, 94.61% are Rh (D) positive whereas only 5.39% are Rh(D) Negative.[3]

A Blood transfusion reaction can be defined as any adverse effect or an undesirable and unintended occurrence during or after transfusion of blood component or products. These adverse effects may manifest as fever and can lead to more serious complications like renal failure, shock and even death. Transfusion of blood has been found to be a safe and effective way to correct haematological deficit. But at the same time it is also important that blood should be used in a judicious way and health care providers must be aware of the risks associated with Blood Transfusion.[4]

Case Summary:

A 32 year old female came to a tertiary level hospital complaining of severe breathlessness, profuse per vaginal bleeding, severe lethargy and altered consciousness on her 3rd POD of LUCS

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conducted at a local hospital in a remote area. She had already received 4 units of "B" positive whole blood on information provided by the patient's relatives, but no documented evidence was shown regarding the patient's blood group. On physical examination, she was pale. Her blood pressure was 80/50 mmHg and pulse rate was 110b/min. On auscultation, her lungs had bilateral basal crepitation. Her oxygen saturation was 92% on room air and her urine output was low. She was admitted to the ICU immediately and routine investigations were sent. The investigations revealed that her Hb% was 4.05gm/dl; WBC was 20000/mm^3 with 85% Neutrophils; ESR -145mm in first hour and platelets 60000/$mm.^3$ Her creatinine was 5.7mg/dl. Her APTT, FDP and Serum Fibrinogen were also markedly increased.

She was immediately started on broad spectrum antibiotics and advised for 3 units of packed cell transfusion. A requisition was given for "B" positive blood. The patient's blood was drawn for cross matching, but the sample was hemolyzed by the time it arrived to the lab. As a prerequisite of cross matching, the blood grouping of the donor and the patient were done. The donor's blood group reaction was "4+"agglutination ("B" positive), but the patient's blood group reaction was "1+" agglutination or mixed field reaction ("B" positive). Cross- matching with the donor's blood with the patient's turned out to be incompatible in both major and minor cross matching procedures. After several attempts to cross match, Coomb's test was done on the patient's sample. The Coomb's test was positive and there was evidence of hemolysis. At the same time Her LDH (lactate de hydrogenase) started to rise and was also several folds above the normal. And the sample tested revealed the blood group to be" B" positive (with mixed field reaction).

Meanwhile, the patient's condition deteriorated and decision was taken to transfuse her with "O" positive washed packed cell and "AB" positive plasma in order to maintain her hemodynamics. The next day, her creatinine shot up to 8.5mg/dl and a hemodialysis was arranged. After the dialysis, grouping was again done on her blood with a fresh sample. This time, on centrifuging the sample, the serum was clear with no signs of hemolysis. The blood group now revealed to be "O" Rh positive in both forward and reverse grouping tests.

The patient was transfused further with 3 units of "O" positive packed cell and 4 units of "AB" positive FFP. She underwent 2 sets of dialysis. Her condition improved gradually with other necessary supportive management. She was discharged with Hb%- 9gm/dl, creatinin-2.6 mg/dl, WBC- 11000/mm^3, Platelets- 150000/mm^4, lungs clear. Finally the patient's blood group was confirmed to be "O"-Rh positive.

Table-I

Blood group of the patient in the first sample

	Cell Groups			Rhesus Groups	Serum Groups		
Test substance	Anti A	Anti B	Anti AB	Anti D	A cell	B cell	O cell
Test results	__	± Mixed field reaction	+ Mixed field reaction	+	Not done	Not done	Not done

Table-II

Blood grouping of patient after hemodialysis.

	Cell Groups			Rhesus Groups	Serum Groups		
Test substance	Anti A	Anti B	Anti AB	Anti D	A cell	B cell	O cell
Test results	__	__	__	+	+	+	+

Discussion:

In ABO mismatched blood transfusion, two types of Acute Transfusion Reaction (ATR) occur:

A. Immunological reactions: Among the various acute immunological reactions like hemolytic, allergic, febrile non hemolytic, anaphylaxis and TRALI; only hemolytic transfusion reaction was seen in our case in spite of major mismatched blood transfusion.

B. Non- immunological reactions: Among the various acute non immunological reactions like marked fever with shock, congestive heart failure, air embolism, hypocalcaemia, hypokalaemia; none of which were sere seen in our case.

Acute Immune Hemolytic Transfusion Reaction follows the major ABO mismatch Blood Transfusion. Here Antigen (Donor Red Blood Cells) and Antibody (Immunoglobulin G or M present in plasma of recipient) react causing rupture of red blood cell (hemolytic reactions) and intravascular clumping of RBC. The wide spread clumping and destruction of recipient's red blood cells, finally leads to the development of Disseminated Intravascular Coagulation (DIC) and other serious effects such as acute renal failure, cardiovascular collapse and death.

The clinical consequences of Hemolytic Transfusion Reaction (HTR) are triggered via several pathophysiological pathways.[5-8] After intravascular RBC destruction, hemoglobin is released into the plasma which remains bound with Haptoglobin, Hemopexin and Albumin. The hemoglobin is further broken down in the reticulo-endothelial system and absorbed by phagocytosis. If this absorption capacity is exceeded, free hemoglobin passes through the glomeruli and is reabsorbed by renal tubule. And when this reabsorption capacity is also exceeded, hemoglobin can be found in the urine (Hemoglobinurea).[9-10]

The hall mark of febrile non-hemolytic reactions is a mild to severe fever that may begin when the transfusion starts or within 2 hours after its completion.[11]

Confirming a hemolytic transfusion reaction requires proof of blood incompatibility and evidence of hemolysis. When such a reaction is suspected, the person's blood is retyped and cross matched with the donor's blood.[11]

After any sign of a hemolytic reaction, the transfusion is stopped immediately depending on the nature of the person's reaction. The health care team should report"transfusion incompatible blood" to the medical staff and ask them to help.

Protocol to be followed during a transfusion reaction:

- Stop transfusion and begin fluid infusion.
- Monitor vital signs every 15-30 minutes, watching out for signs of shock.
- Maintain an open intravenous line with normal saline solution.
- Insert an indwelling urinary catheter and monitor intake and output.
- Check for signs of DIC.
- Administer drugs such as intravenous medications to raise blood pressure and normal saline solution to combat shock. Adrenaline to treat shortness of breath and wheezing, corticosteroids to reduce inflammation. Furosemide to maintain urinary function. Parenteral antihistamine and corticosteroids are given for allergic reaction.

At the same time, the following examinations should be performed.

- Reexamine blood type of both patient pre-transfused blood sample and donor blood.
- Check for hemolysis, renal function and DIC.[11]

In this case, the patient's hemoglobin was low, so transfusion was needed. But we could not confirm the blood grouping with the first sample because the sample was hemolyzed. Therefore in this situation, we decided to transfuse the patient with "O" positive Packed Cell (washed) and "AB" Positive Plasma. So, neither "A" and "B" antigen nor any Anti "A" and Anti "B" antibody would enter the blood stream. And we got successful result after transfusion and hemodialysis. The patient's Hb% started to raise gradually, creatinine started to fall and the patient's blood samples became clear and normal (no evidence of hemolysis).

When the blood grouping was performed again (both forward and reverse), the result found was "O" Rh Positive. Therefore the patient was diagnosed as a case of "Mismatched Blood Transfusion".

Conclusion:

Transfusion errors are mainly due to transfusion of a wrong blood bag or transfusion to a wrong patient. Therefore to prevent ABO incompatible transfusion, identification of the patient and the blood bag are very important before transfusion as well as blood grouping by forward and reverse must be done for every patient to prevent errors. Cross matching by Indirect Coomb's test is also mandatory.

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INSTRUCTION TO AUTHORS ABOUT UNIFORM MANUSCRIPT WRITING

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