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Chest Heart Journal
Vol. 41, No. 2, July 2017

EDITORIAL

Current status of Interventional Pulmonology and Future Direction

[Chest Heart Journal 2016; 41(2) : 83-85]

The field of interventional bronchoscopy is rapidly expanding and has emerged as an exciting subspecialty in pulmonary medicine. Interven-tional pulmonology offers new approaches to the management of variety of conditions including pleural disease, pulmonary lesion, thoracic malignancy, airway obstruction due to other causes, asthma and COPD[1].

Current status of Interventional pulmonology started in the second decade of the twenty first century. Guideline from ATS/ERS and ACCP were based on expert consensus[2]. But now after a decade it remains valid and continue to reflect much of the current practice. Four recent advances in technology are extending the reach of interventional pulmonology procedures:

- Endobronchial ultrasound system (EBUS): An ultrasound probe on the tip of a bronchoscope allows Interventional pulmonologist to biopsy lymph nodes with more precision. Linear EBUS is quickly becoming the standard of care for mediastinal staging of patients with lung cancer and for sampling mediastinal lymph node. Although this procedure can and should be performed by most bronchoscopist , the Interventional pulmonologist can take the lead in incorporating EBUS into day-to-day practice. In addition to its role as a staging instrument linear EBUS-TBNA is being used to obtain more tissue in advanced or recurrent lung cancer cases to guide targeted lung cancer therapy in the new Era of personalized cancer therapy[3].
- Electromagnetic navigation bronchoscopy : An advanced system that guides the bronchoscope farther than traditional bronchoscopy allows. This system permits biopsy of hard-to-reach abnormal areas of the lung, which would otherwise require more invasive testing. As the clinical presentation of lung cancer has shifted from central squamous cell carcinoma to predominantly peripheral adenocarcinoma there has been an increasing use of Interventional pulmonology techniques to diagnose peripheral lesion . Electromagnetic navigation bronchoscope are being used to obtain tissue from peripheral lesion[4]. They are in competition with transthoracic needle aspiration performed by interventional radiologist.
- Bronchial thermoplasty is an interventional pulmonology procedure for certain patients with severe asthma that cannot be controlled with medication. Through the fiber optic bronchoscope Interventional pulmonologist applied heat probe to the wall of airway. The heat destroys the smooth muscle layers of airways whose constriction contributes to asthma symptoms[5].
- Endobronchial valve placement: This can be performed for persistent postoperative air leak and also for bronchoscopic lung volume reduction (BLVR) a less invasive alternative to lung volume reduction surgery[6].

Current status of Interventional pulmonology in Bangladesh is not satisfactory. As Interventional pulmonology instrumentation is very expansive, availability of advance bronchoscopy suit is limited both in public and private sector[7]. Interventional pulmonology practitioner is also limited because lack of facilities of organized training program and absence of Interventional pulmonology fellow ship course. EBUS and Autofluorescence bronchoscopy started in 2010 only in single public institution. Cryotherapy and Argon plasma coagulation is also performing in limited center. Conventional TBNA and pleuroscopy is being done as wide spectrum. Foreign body removal from the tracheo bronchial tree using flexible bronchoscope is almost regular practice.

Two most important Interventional pulmonology practice in Bangladesh is promising. One is trachiobronchial stenting which give relief of patient from stenosis of the tracheobronchial tree from chronic disease, long standing intubation in ICU patients, disorganized cartilage, and in case of tracheobronchial fistula. Another is Indwelling pleural catheter which is very much effective procedure for recurrent malignant pleural effusion . TIPC is usually used but some center where indwelling catheter kit is not available modified way it can be done using central venous catheter kit which can be kept in situ for 3-4 weeks and aspiration cane done when there is accumulation of pleural fluid in the space.

Although interventional pulmonology procedures carry low risks, they are not risk-free. Uncommon complications of interventional pulmonology procedures include:-Pneumothorax, Bleeding, Over sedation, leading to pneumonia or the need for temporary life support. Interventional pulmonology procedures are generally safer and have a shorter recovery time, compared to surgery. However, surgery remains the best option for diagnosis and treatment of many lung conditions.

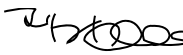
The future of interventional pulmonology

The future of Interventional pulmonology seems to be very bright. As the lung cancer epidemic continues, except only slightly decreasing trends in developed countries but on the rise in developing countries. For the fore seeable future, patients will continue to present with cancerous central airway lesion that require ablative therapy or stenting . EBUS is both for staging and diagnosis and is rapidly being brought from the academic center to the community. Interventional pulmonology instrumentation is expansive so major concern is what to do in developing countries, where lung cancer is being diagnosed more frequently. Volunteerism on the part of Interventional pulmonology trained personal and generosity on the part of industrialist will remain the only means of transporting Interventional pulmonology to developing countries for the fore seeable future.

In future Interventional pulmonology practice must become more evidence based . Most of the medical literature in Interventional pulmonology is from single institutional case series. But now Interventional pulmonology research is shifting to randomized controlled multicenter studies, often with sham controls (5,6). This type of research can best serve patients and can only lead to improve the status of Interventional pulmonology within the medical world.

Although it was relatively easy to define IP, it remains difficult to define at present who is an interventional pulmonologist. This is an important question that needs to be defined in future. Possibly a board exam will help to answer the question but that seems many years away in Bangladesh where there is no handsome number of Interventional pulmonology Skill persons. In addition to acquiring procedural skill, Interventional pulmonology fellows must develop knowledge based on area such as thoracic malignancy, complex airway disorder, and pleural diseases[8]. Interventional pulmonology required more training and experience than is available in Bangladesh in most pulmonary and thoracic surgery residency.

We have been fortunate enough to be involved with the Interventional pulmonology community since the beginning. Over last 10 years we have collaborated with and become friends with many Interventional pulmonology practitioners from deferent countries. Interventional pulmonology is an international specialty. The diseases that Interventional pulmonology confronts are global and in future we must make sure that the care Interventional pulmonology offers is also global.



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Chest Heart Journal
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ORIGINAL ARTICLE

Outcome of Prolonged Cardiopulmonary Bypass Time (CPBT) on Renal Function in Patients Undergoing Open Heart Surgery

Md. Shafiqul Islam[1] , Subhash Ch. Mandal[2], Md. Mofizur Rahman Mia[3], Saiful H. Talukder[4]

Abstract:

Objective: *To observe changes of renal function from the preoperative period to that of the postoperative period in cardiac surgical patients with prolonged cardiopulmonary bypass time.*

Background: *Cardiopulmonary bypass (CPB) is considered responsible for kidney damage. By using markers like blood urea, serum creatinine, creatinine clearance rate and 24 hours urine output we assessed whether the length of CPB influences kidney function.*

Methods: *60 consecutive cardiac operation patients with CPB time of more than 90 minutes were studied. Blood urea, serum creatinine, creatinine clearance rate and 24 hours urine output was measured preoperatively and on the 1st, 2nd and 7th postoperative days in the intensive care unit.*

Result: *Acute renal failure developed in 5 patients (8.3%). Dialysis for acute renal failure was required in 2 (3.33 %) patients. Deep sternal wound infection occurred in 5 patients (8.3%). Respiratory tract infection developed in 6 (10 %) patients. No patient required prolonged ventilation > 48 hours. One patient (1.66%) died on 6th post operative day (POD) due to multi organ failure.*

Conclusion: *Patients with prolonged cardiopulmonary bypass time have detrimental effect on renal function with some other mortality and morbidity in the perioperative period.*

Key words: *Cardiopulmonary bypass, Cross clamp time, Extracorporeal circulation time.*

[Chest Heart Journal 2017; 41(2) : 87-93]

Introduction:

Cardiopulmonary bypass (CPB) is a technique by which pumping action of the heart and the gas exchange functions of the lungs are replaced temporarily by a mechanical device, the pump oxygenator, attached to a patient's vascular system. CPB represents one of the most important biomedical inventions in the history of health care[1]. About 80% of routine cardiac surgical procedures are performed world wide using CPB[2].

Renal dysfunction in the postoperative period of open heart surgery is a risk factor for hospital mortality[3,4]. It is a frequent complication in the postoperative period of open heart surgery with a reported incidence of between 1% and 31%. [5,6]

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Incidence of acute renal failure (ARF) requiring dialysis is 0.7%- 5% and mortality rate of patients with ARF after open heart surgery is 28%-63%.[7]

The goal of CPB is to maintain regional perfusion at a level that supports optimum cellular and organ function. Thus any decrease in renal perfusion during CPB depending upon its magnitude and duration can lead to significant cellular injury [8].

Prolonged CPB time is defined as extra corporeal circulation time longer than 80 minutes[9] or, it is longer than 98 minutes [10-11]. Adhesion of blood corpuscles to endothelial cells are increased producing progressive alteration of renal plasma flow by increased duration of CPB[12].

It has been shown that inflammatory response increases significantly beyond 80 minutes of CPB time. As degree of inflammation appears to be correlated with alterations in the organ function, CPB time of more than 80 minutes may affect splanchnic organ function more pronouncedly than CPB time less than 70 minutes[13].

National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh has been performing the central role in the field of cardiac surgery in our country. This study was designed with the objective to evaluate the influence of prolonged cardiopulmonary bypass time on renal function on patients of open heart surgery in NICVD. This will contribute to develop strategies for prevention of renal complications following open heart surgery at NICVD.

Materials and methods

This cross sectional study was done in the National Institute of Cardiovascular Diseases (NICVD), Dhaka from January 2015 to December 2016.

Patients undergoing cardiac surgery under CPB were enrolled in this study. Their renal functions were evaluated by obtaining blood sample preoperatively as well as postoperatively on 1st POD, 2nd POD and on 7th POD. Normal preoperative values of Blood urea, Serum creatinine, Creatinine clearance rate and 24 hours urine output was considered as parameters for evaluation of renal function. Known case of renal dysfunction (S.creatinine >1.5 mg/dl), Patients with uncontrolled diabetes mellitus, hypertension and patients needing re-establishment of CPB were excluded from the study.

During peroperative period, operation type, extracorporeal circulation time, Cross clamp time, Mean arterial blood pressure, CVP and total ICU stay were recorded in each patient.

All the relevant collected data are compiled on a master sheet first and then organized by using scientific calculator and standard statistical formulas. Statistical analyses of the result were done by computer software device as statistical packages for social scientist (SPSS).The results were presented in tables, figures and diagrams etc. To see correlation between prolonged cardiopulmonary bypass time and renal function, the study outcomes were evaluated regarding unpaired 't' test and multiple regression analysis was done. A "p" value <0.001 was considered as significant.

Results:

Base line biochemical variables:

The data of clinical findings shows the base line values of blood urea, serum creatinine, creatinine clearance rate and 24 hours urine output of the study population measured preoperatively. Blood urea (mg/dl), serum creatinine (mg/dl), creatinine clearance rate(ml/min),and 24 hours urine output (ml) was 32.70 ± 8.35, 0.87 ± 0.20, 83.21 ± 06.03 and 1680.37 ± 214.63 respectively.

Table-I

Distribution of study subjects by baseline biochemical variables

Baseline biochemical variables	Mean ± SD
Blood urea (mg/dl)	32.70 ± 8.35
Serum creatinine (mg/dl) rate	0.87 ± 0.20
Creatinine clearance (ml/min)	83.21 ± 06.03
24 hours urine output (ml)	1680.37 ± 214.63

Per operative variables:

The mean extracorporeal circulation time or cardiopulmonary bypass time (CPBT) was 103.07 ± 50.12 min and mean cross clamp time (XCT) was 63.81 ± 30.66 min.

Table-II

Distribution of study subjects by per operative variables

Per operative variables	Mean ± SD
Extracorporeal circulation time (min)	103.07 ± 50.12
Cross clamp time (XCT) (min)	63.81 ± 30.66

Post operative variables of the patients:

The Mean ± SD of duration of mechanical ventilation was 10.37 ± 2.58 hours, Mean ± SD of ICU stay was 3.83 ± 1.37 days and the Mean ± SD of duration of hospital stay was 10.37 ± 2.58 days.

Table-III

Comparison of postoperative events

Variables	Mean ± SD
Period of mechanical ventilation (hours)	13.61 ± 4.45
ICU stay (days)	3.83 ± 1.37
Total hospital stay (days)	10.37 ± 2.58

Correlation between renal parameters in different postoperative days (POD) and Cardiopulmonary bypass time (CPBT):

a) Correlation between blood urea in different postoperative days (POD) and Cardiopulmonary bypass time (CPBT):

Preoperative blood urea was with in normal limit. Mean ± SD blood urea level was32.70 ± 8.35 mg/dl.

By the 1st postoperative day (POD1) blood urea levels were recorded and it was found that the Mean ± SD blood urea level was 67.12 ± 8.81 mg/dl.

On the 2nd post operative day (POD2) Mean ± SD blood urea level was 77.38 ± 10.40 mg/dl.

Similarly, on the 7th postoperative day (POD7) Mean ± SD of blood urea level was 53.07 ± 15.17 mg/dl.

The table shows significant correlation between CPBT and blood urea in different post operative days where, r = .609, .665 and .753 respectively and p value was significant (<.001) in different post operative days.

Table 5: Correlation between serum creatinine (mg/dl) in different postoperative days and Cardiopulmonary bypass time (CPBT):

b) Correlation between serum creatinine (mg/dl) in different postoperative days and Cardiopulmonary bypass time (CPBT):

Preoperative serum creatinine was with in normal limit. Mean ± SD serum creatinine level was .87 ± .20 mg/dl.

By the 1st postoperative day (POD1) serum creatinine levels were recorded and it was found that the Mean ± SD serum creatinine level was 2.36 ± .49 mg/dl.

On the 2nd post operative day (POD2) serum creatinine levels were recorded and was found that Mean ± SD serum creatinine level was 2.41 ± .76 mg/dl.

Similarly, on the 7th postoperative day (POD7) Mean ± SD of serum creatinine level was 1.55 ± 1.03 mg/dl.

The table shows significant correlation between CPBT and serum creatinine in different post operative days where, r = .421, .398 and .436 respectively and p value was <.001 in different post operative days.

c) Correlation between creatinine clearance rate (CCr) (ml/min) in different postoperative days and Cardiopulmonary bypass time (CPBT):

Preoperative creatinine clearance rate (CCr) was with in normal limit. Mean ± SD creatinine clearance rate (CCr) level was 83.21 ± 6.03 ml/min.

By the 1st postoperative day (POD1) creatinine clearance rate (CCr) levels were recorded and it was found that the Mean ± SD creatinine clearance rate (CCr) was 43.97 ± 7.24 ml/min.

On the 2nd post operative day (POD2) creatinine clearance rate (CCr) were recorded and was found that Mean ± SD creatinine clearance rate (CCr) was 44.23 ± 4.85 ml/min.

Similarly, on the 7th postoperative day (POD7) Mean ± SD of creatinine clearance rate (CCr) was 72.96 ± 11.84 ml/min.

The table shows significant negative correlation between CPBT and creatinine clearance rate (CCr) in different post operative days where, r = -.609, -.640 and -.723 and p value was <.001 in different post operative days.

d) Correlation between 24 hours total urine output (ml) in different postoperative days and Cardiopulmonary bypass time (CPBT):

Preoperative 24 hours total urine output (ml) was within normal limit. Mean ± SD 24 hours total urine output (ml) was 1680.37 ± 214.63.

By the 1st postoperative day (POD1) 24 hours total urine output (ml) were recorded and it was found that the Mean ± SD 24 hours total urine output (ml) was 1546.15 ± 225.78.

On the 2nd post operative day (POD2) 24 hours total urine output (ml) were recorded and was found that Mean ± SD 24 hours total urine output (ml) was 1507.60 ± 278.62.

Similarly, on the 7th postoperative day (POD7) Mean ± SD 24 hours total urine output (ml) was 1624.67 ± 386.30.

The table shows significant negative correlation between CPBT and 24 hours total urine output (ml) in different post operative days where, r = -.421, -.511 and -.448 and p value is <.001 in different post operative days.

Table-IV

Comparison of post operative complications

Acute renal failure	No	Percentage
Yes	5	8.3
No	55	91.6
Need for dialysis		
Yes	2	3.33
No	58	96.66
Deep sternal wound infection		
Yes	5	8.3
No	55	91.6
Respiratory tract infection		
Yes	6	10
No	54	90
prolonged ventilation > 48 hours		
Yes	0	0
No	60	100
Death		
Yes	1	1.66
No	59	98.33

Comparison of post operative complications: Acute renal failure developed in 5 patients (8.3%). Dialysis for acute renal failure was required in 2 (3.33 %) patients. Deep sternal wound infection occurred in 5 patients (8.3%). Respiratory tract infection developed in 6 (10 %) patients. No patient required prolonged ventilation > 48 hours. One patient (1.66%) died on 6th POD due to multi organ failure.

Table-V

Multiple regression analysis considering Cardiopulmonary bypass time (CPBT) as dependent variable and age, sex and blood urea as independent variable

Variable	Standardized Coefficients (β)	p value	95% Confidence Interval for β	
			Lower Bound	Upper Bound
(Constant)		.005	-86.275	-16.051
Age	.326	<.001	.530	1.601
Sex	.096	.215	-5.710	24.790
Blood urea	.637	<.001	1.506	2.545

The above table shows significant correlation of age and blood urea with cardiopulmonary bypass time. p value is <.001 for each variable.

Table-VI

Multiple regression analysis considering Cardiopulmonary bypass time (CPBT) as dependent variable and age, sex and Creatinine clearance rate (CCr) as independent variable:

Variable	Standardized Coefficients (β)	p value	95% Confidence Interval for β	
			Lower Bound	Upper Bound
(Constant)		.000	175.057	305.797
Age	.334	<.001	.523	1.659
Sex	.105	.201	-5.709	26.543
CCr	-.603	<.001	-3.283	-1.820

The above table shows significant correlation of age and Creatinine clearance rate (CCr) with cardiopulmonary bypass time. p value is <.001 for each variable.

Table-VII

Multiple regression analysis considering Cardiopulmonary bypass time (CPBT) as dependent variable and age, sex and Serum Creatinine as independent variable

Variable	Standardized Coefficients (β)	p value	95% Confidence Interval for β	
			Lower Bound	Upper Bound
(Constant)		309	-18.216	56.545
Age	.489	<.001	.923	2.274
Sex	.065	.525	-13.778	26.685
S. creatinine	.337	<.001	6.350	26.397

The above table shows significant correlation of age and serum creatinine with cardiopulmonary bypass time. p value is <.001 for each variable.

Table-VIII

Multiple regression analysis considering Cardiopulmonary bypass time (CPBT) as dependent variable and age, sex and 24 hours urine output as independent variable

Variable	Standardized Coefficients (β)	p value	95% Confidence Interval for β	
			Lower Bound	Upper Bound
(Constant)		.001	45.386	173.339
Age	.459	<.001	.789	2.212
Sex	.083	.427	-12.389	28.869
24 hrs urine output	-.305	<.001	-.068	-.011

The above table shows significant correlation of age and 24 hrs urine output with cardio-pulmonary bypass time. p value is <.001 for each variable.

Discussion:

The patients were stratified in the following age groups: 30 years and less, 31-40 years, 41-50 years and more than 50 years. (Shown in table 1). Maximum numbers (33) of cases (55%) were found in <30 years of age group followed by 16.7% (10) between 41-50 years, 15% (9) more than 50 years and 13.3% (8) 41-40 years. About 52% (31) were female and about 48% (29) were male in the study population.

Most (46.7%) of patients had repair of congenital anomalies, 20% experienced mitral valve replacement, 13.3% CABG, 13.3% aortic valve replacement, CABG with MVR, CABG with DVR and repair of RASV each comprised of 1.7%.

Based on preoperative (baseline) biochemical variables it has been shown that blood urea, serum creatinine, creatinine clearance and 24 hours urine output were within normal value. Among the peroperative variables, the mean extracorporeal circulation time (ECCT) and mean cross-clamp time (XCT) were recorded for each patients.

Renal function was assessed by measuring blood urea, serum creatinine, creatinine clearance and 24 hours urine output. Parameters were evaluated preoperatively and postoperatively on 1st, 2nd and 7th POD. The mean blood urea was 32.70 ± 8.35 mg/dl at baseline which increased sharply to 67.12 ± 8.81 mg/dl at 1st POD and then insidiously to 77.38 ± 10.40 mg/dl at 2nd POD and then decline steeply to 53.03 ± 15.75 mg/dl at 7th POD. The difference of blood urea level in different postoperative days was found statistically significant. Similar types of results were observed [8].

Mean preoperative serum creatinine level was 0.87 ± 0.20 mg/dl. Mean serum creatinine level in the 1st POD, 2nd POD and 7th POD showed significantly higher levels. Here the difference in the postoperative values was statistically significant. A study found that serum creatinine levels increased progressively in both groups from preoperatively to 24 hours postoperatively and there after decreased by 48 hours post operatively.[9] This finding was similar to our observation.

Comparison of creatinine clearance rate (ml/min) was also evaluated preoperatively and on different postoperative days. But significant differences were found in values on 1st, 2nd and 7th postoperative days.

Comparison of 24 hours urine output (ml) were done preoperatively as well as in different post operative days. Here it was observed that in all the periods 24 hours urine output was lower significantly in the post operative periods.

Besides comparing renal parameters time course of renal variables were also observed. Regarding blood urea levels, in course of time values increased on 1st and 2nd POD, declines on consecutive POD but remains elevated in some

cases. But statistically significant difference remained between preoperative blood urea level and value on 7th POD.

Trend of change of serum creatinine level was observed in patients with CPBT >90 min. Serum creatinine was increased on 1st POD. There after creatinine value declined to some extent and did not reach the preoperative value. At each time point (2nd and 7th POD) creatinine value remained elevated. There was highly significant difference between preoperative and 7th POD serum creatinine value.

Change of creatinine clearance rate (CCr) over each point of time was observed. During the postoperative period CCr reduced significantly on 1st and 2nd POD. There after CCr gradually increased over time from 1st POD to 7th POD, but reached a level below the preoperative level.

Several post operative variables have been observed (Shown in Table 10). In this study mean ventilation period 13.61 ± 4.45 hours. Procedures having CPBT <90 minutes are to be better tolerated by the patients; ventilation time was significantly higher in patients with CPBT> 90 minutes.

On the other hand, mean period of total ICU stay were 3.83 ± 1.37 days. These findings were similar to other study where high CPBT group required more ICU stay[8].

Total postoperative hospital stay was10.37 ± 2.58 days, similar to reported length of hospital stay 7.36 ± 3days and 5.84 ± 1.5 days in long CPBT group vs. short CPBT group respectively[9-11]. It was statistically significant (p<0.03).This finding corresponds to our study.

Thus the period of mechanical ventilation, ICU stay, and total postoperative hospital stay were greater. All these reflect definite clinical advantage as well as favorable economic outcome associated with CPBT <90 minutes[12]

In this cross sectional study, the patient was followed up to 30 days. Among the total 60 patients, one patient died on 6th POD due to multi organ failure. Mortality rate was 1.66%.

In the present study, postoperative morbidities were acute renal failure (8.3%), need for dialysis (3.3%), deep sternal wound infection (8.3%), respiratory tract infection (10%). None of them required prolonged ventilation (>48 hours). A study showed that renal complication was 5.4% vs. 3.3%, prolonged ventilation was 6.6% vs. 3.7% in prolonged vs. short CPBT groups respectively[9].Another study reported acute renal failure (15.8% vs. 5.9%), infective complication (7.42% vs. 5.9%) in two groups respectively[13].

The above discussion shows prolonged cardiopulmonary bypass time has statistically significant impact on renal function and post operative morbidity and mortality. The renal parameters showed significant difference in different post operative periods with evidence of significant impact on post operative outcome. So, our data furnish substantial evidence that CPBT> 90 minutes confer significant impact on renal function and postoperative morbidity and mortality.

Conclusion:

This cross sectional study on open heart surgery patients having prolonged cardiopulmonary bypass time revealed significant difference in renal parameters on different postoperative days. The trend of changes in renal parameters on different postoperative days with relation to CPBT. Cardiopulmonary bypass time has more detrimental effect on renal function and requires longer duration of ICU stay and hospital stay and increased incidence of deep sternal wound infection and respiratory tract infection in patients with CPBT > 90 minutes. So, it can be concluded that less cardiopulmonary bypass time offers better preservation of renal function as well as better early post operative outcome in open heart surgery patients.

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ORIGINAL ARTICLE

Comparative Study of Ambrisentan and Sildenafil on Surgical Outcome in Left to Right Shunt Anomaly Patients with Pulmonary Hypertension

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Abstract:

Background: *Pulmonary hypertension is common in patients with atrial septal defect, ventricular septal defect and patent ductus arteriosus. Closure of large left to right cardiac shunts with preexisting significant pulmonary arterial hypertension is usually accompanied by hazards of post-operative residual pulmonary arterial hypertension, pulmonary hypertensive crisis and right ventricular dysfunction. Pulmonary vasodilator drugs should be used in left to right shunt anomaly patients with pulmonary hypertension for reduction of pulmonary hypertension and should be continued postoperatively for better surgical outcome. This study compares short term surgical outcome of left to right shunt anomaly patients with pulmonary hypertension between preoperative and postoperative therapy with ambrisentan and sildenafil.*

Methods: *The study was conducted in the department of cardiac surgery of Bangabandhu Sheikh Mujib Medical University and National Institute of Cardiovascular Diseases (*NICVD*) from February 2014 to February 2016 in left to right shunt atrial septal defect or ventricular septal defect or patent ductus arteriosus patients with moderate to severe pulmonary hypertension. Among 40 patients; 20 patients of group-1 recei-ved ambrisentan and another 20 patients of group-2 received sildenafil during pre-operative and postoperative period up to 3 months. Colour Doppler echocardiography was used to measure pulmonary artery systolic pressure in both groups except per operative pulmonary artery systolic pressure which was measured directly by pulmo-nary arterial line. Recorded pulmonary artery systolic pressure, cardiopulmonary by-pass time, duration of mechanical ventilation time and death were compared between two groups. Data were presented as Mean ± SD. Differences between two groups were compared using chi-square and* t *test. P value less than 0.05 was considered to be significant.*

Results: *The mean difference of pulmonary artery systolic pressure after admission and 15 days after starting medication were statistically not significant between two groups ($p > 0.05$). Reduction of pulmonary artery systolic pressure after correction (Post by-pass) were occurred in both groups. But the mean difference of pulmonary artery sys-tolic pressure after correction (Post bypass) was statistically not significant beween the two groups ($p > 0.05$). Ambrisentan group showed more reduction of pulmonary artery systolic pressure postoperatively than sildenafil group. Postoperatively signi-ficant shortened cardiopulmonary bypass time and mechanical ventilation time was found in ambrisentan group in comparison to sildenafil group.*

Conclusions: *Ambrisentan has better surgical outcome than sildenafil in left to right shunt ano-maly patients with moderate to severe pulmonary hypertension.*

Key words: *Ambrisentan, Left to right shunt anomaly, Pulmonary hypertension, Sildenafil.*

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Introduction:

Pulmonary hypertension is common in patients with adult congenital heart disease (about 10%). Congenital heart defects leading to pulmonary hypertension can be simple (atrial septal defect, ventricular septal defect, patent ductus arteriosus) or complex (atrioventricular septal defect, truncus arteriosus).[1] It has been possible to reduce pulmonary vascular resistance because of improvement in pulmonary vaso-dilators and more widespread use of pulmonary vasodilators. Then patient with pulmonary arterial hypertension are amenable to surgery.[2] Recent advances in pedi-atric cardiac surgery techniques have increased ability to correct congenital heart disease at an early age.[3]

The pathogenesis of pulmonary hypertension (PH) is complex and multifactorial. Increased pulmonary arterial pressure (PAP) in patients with pulmonary hypertension probably results from combination of pulmonary vasoconstriction, inward vascular wall remodelling and in situ thrombosis.[4]

Affinity of ambrisentan for ETA receptor is >4000-fold than affinity for ETB recep-tor. Administration of ambrisentan in patients with pulmonary arterial hypertension is associated with vascular smooth muscle relaxation and vasodilatation. Bosentan, another ET-1 receptor antagonist, has 100 times greater affinity for ETA receptor than for ETB receptor. So, ambrisentan is more specific ETA-receptor antagonist than bosentan.[5]

"Food and Drug Administration" approved ambrisentan in June 2007.[4] (Wal et al., 2013). Ambrisentan was approved in United States in 2007. Ambrisentan was later approved for use in Canada (In 2008), Europian Union (In 2008), New Zealand (In 20109), Australia (In 2009) and Japan (In 2010).[6] The current approved dose of ambrisentan is 5 mg once daily which can be increased to 10 mg once daily when the drug is tolerated at the initial dose.[7] In the clinical setting, pediatric patients can be started on ambrisentan at the initial 2.5 (<20 kg) or 5 mg dose (>_20 kg) and considered for an up-titration to the 5–10 mg dose.[8] Dose of ambrisentan incase of adult over 18 years is 5 mg once daily and can be increased to 10 mg once daily if necessary.[9] Ambrisentan is highly bound to plasma proteins (99%). Elimination is mostly through biliary system with majority of oral doses recovered in urine and feces. Ambrisentan half life ranges from 13.6 to 16.5 hours.[10]

Sildenafil has been used to treat pulmonary hypertension in both pediatric and adult patients that have undergone cardiac surgery.[11] Sildenafil increases effects of locally produced nitric oxide (NO) by inhibiting break-down of cyclic guanosine mono-phosphate. This results in pulmonary vasodilation and inhibition of smooth muscle cell growth.[12] Dose of of sildenafil is 20 mg 3 times daily.[9] Sildenafil was approved by European Medicines in 2011. Dose of sildenafil is 10 mg 3 times daily for weight less than 20 kg and 20 mg 3 times daily for weight equal and more than 20 kg.[13] Half-life of sildenafil is approximately 4 hours and bioavailability is approximately 40% which is reduced to 29% following a large meal.[14] The most serious adverse effects of sildenafil are arrhythmias, heart block, cardiac arrest, stroke and hypotension.[15]

Closure of large left to right cardiac shunts with preexisting significant pulmonary ar-terial hypertension is usually accompanied by hazards of post-operative residual pulmonary arterial hypertension, pulmonary hypertensive crisis and right ventricular dysfunction.[16] The goal of perioperative pulmonary arterial hypertension therapy is to maximize pulmonary vasodilatation and reduce pulmonary vascular resistance. This decreases right ventricular afterload and subsequently improves cardiac output.[11]

Pulmonary vasodilator drugs should be used in left to right shunt anomaly patients with pulmonary hypertension for reduction of pulmonary hypertension and should be continued postoperatively for better surgical outcome. It should be known which pulmonary vasodilator drug has better surgical outcome in left to right shunt anomaly patients with pulmonary hypertension. The aim of this study is to compare short term surgical outcome of left to right shunt anomaly patients with pulmonary hypertension between preoperative and postoperative therapy with ambrisentan and sildenafil.

Materials and methods:

This clinical observational study was conducted in the department of cardiac surgery of Bangabandhu Sheikh Mujib Medical University and National Institute of Cardio-vascular Diseases (*NICVD*) from February 2014 to February 2016 in left to right shunt atrial septal defect or ventricular septal defect or patent ductus arteriosus patients with pulmonary

arterial systolic pressure 50 to 100 mm Hg. The per-mission from the institutional review board of Bangabandhu Sheikh Mujib Medi-cal University (BSMMU) and informed consent from all patients were obtained for this study. Among 40 patients; 20 patients of group-1 received ambrisentan and another 20 patients of group-2 received sildenafil during preoperative and post-operative period.

Preoperatively ambrisentan was given to group-1 patients via oral route at a dose of 2.5 mg in <20 kg case and 5 mg in >_20 kg case once daily. Sildenafil was given to group-2 patients via oral route 25 mg 3 times daily in adult or 0.5 mg/ kg in pedi-atric case in every 8 hourly for 15 days with the final dose 8 hours before induction of anaesthesia. Postoperatively patients of group-1 were got ambrisentan and patients of group- 2 were got sildenafil from the day of operation in intensive care unit via nasogastric tube till extubation and then via oral route after extubation up to 3 months postoperatively.

Pulmonary artery systolic pressure were measured after admission, 15 days after starting medication, before correction (Prebypass), after correction(Post bypass), at 7th post-operative day, at 1 month after operation and at 3 month after operation in both groups.

Colour Doppler echocardiography was used to measure pulmonary artery systolic pressure in both groups except per operative pulmonary artery systolic pressure. Per operative pulmonary artery systolic pressure was measured directly by pulmonary arterial line. Recorded pulmonary artery systolic pressure, cardiopulmonary bypass time, duration of mechanical ventilation time and death were compared between two groups. Data were presented as Mean ± SD. Differences between two groups were compared using chi-square and Student's t-test. P value less than 0.05 was considered to be significant.

Results:

Total number of 40 (Forty) patients were selected for the study. There were two groups; group-1 and group -2. Among 40 patients; 20 patients were in group-1 and 20 patients were in group-2. All patients of group-1 received ambrisentan and all patients of group-2 received sildenafil during preoperative and postoperative period. The findings of the study obtained from data analysis are presented below.

Age distribution of the selected patients between group-1 and group-2 are showed in table-I. The mean age in group-1 was 24.85±13.98 and in group-2 was 20.8±12.19. It was observed that mean age was not significantly different bet-ween two groups (p> 0.05).

Table-I

Comparison of age between two groups

Variable	Group 1 (n=20)	Group 2 (n=20)	P value
Age	Mean±SD 24.85±13.98	Mean±SD 20.8±12.19	0.33 ^{ns}

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was p< 0.05.
n=number of subjects; ns= Not significant.

Sex distribution of the selected patients between group-1 and group-2 are showed in table-II. It was found that 20% were male and 80% were female in group-1. In group-2, 25% were male and 75 % were female. There was no significant difference in sex distribution between two groups (p> 0.05).

Weight distribution of the selected patients between group-1 and group-2 are showed in table-III. Mean weight in group-1 was 40.8±15.55 and in group-2 was 38.25±16.03. It was observed that mean weight was not significantly different between two groups (p> 0.05).

Table-II

Comparison of sex between two groups

Sex	Group-1(n=20)		Group-2(n=20)		P value
	Number	Percentage	Number	Percentage	
Male	4	20%	5	25%	0.70^{ns}
Female	16	80%	15	75%	
Total	20	100%	20	100%	

Data were expressed as number and percentage.
Statistical analysis were done by Chi-square test. Level of significance was p< 0.05.
n=number of subjects; ns= Not significant.

Table-III

Comparison of weight between two groups

Variable	Group 1 (n=20)	Group 2 (n=20)	P value
Weight(Kg)	Mean±SD 40.8±15.55	Mean±SD 38.25±16.03	0.61 ns

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was p< 0.05.
n=number of subjects; ns= Not significant.

Type of operation performed between two groups are shown in table-IV. In group-1 80% ASD (Atrial septal defect) closure , 15% VSD (Ventricular septal defect) closure and 5% PDA(Patent ductus arteriosus) ligation were done. In group-2 75% ASD (Atrial septal defect) closure , 20 % VSD (Ventricular septal defect) closure and 5% PDA(Patent ductus arteriosus) ligation were done. There was no significant difference in type of operation performed between two groups (p> 0.05).

Table-IV

Comparison of type of operation performed between two groups

Variable	Group-1 N=20		Group-2 N=20		P value
	Number	%	Number	%	
ASD	16	80%	15	75%	0.92 ns
VSD	3	15%	4	20%	
PDA	1	5%	1	5%	
Total	20	100%	20	100%	

Data were expressed as number and percentage.
Statistical analysis were done by Chi-square test. Level of significance was p< 0.05.
n=number of subjects; ns= Not significant.

Table-V shows pulmonary artery systolic pressure after admission in two groups. Mean pulmonary artery systolic pressure after admission in group-1 was 68.45 ± 11.57 and 68.95±11.01 in group-2. The mean difference of pulmonary artery systolic pressure after admission was statistically not significant between the two groups (p > 0.05).

Table-V

Comparison of Pulmonary artery systolic pressure after admission between two groups:

Variable	Group 1 (n=20)	Group 2) (n=20)	P value
Pulmonary artery systolic pressure after admission	Mean ± SD 68.45 ± 11.57	Mean±SD 68.95±11.01	0.89 ns

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was p< 0.05.
n=number of subjects; ns= Not significant.

Table-VI compares pulmonary artery systolic pressure 15 days after starting medi-cation between two groups. Mean pulmonary artery systolic pressure 15 days after starting medication in group-1 was 60.7±10.91 and in group-2 was 63.3±9.88. Reduction of pulmonary artery systolic pressure 15 days after starting medication were occurred in both group. But the mean difference of pulmonary artery systolic pressure 15 days after starting medication was statistically not significant between the two groups (p > 0.05).

Table-VI

Comparison of pulmonary artery systolic pressure 15 days after starting medication between two groups

Variable	Group 1 (n=20)	Group 2) (n=20)	P value
Pulmonary artery systolic pressure 15 days after starting medication	Mean±SD 60.7± 10.91	Mean±SD 63.3±9.88	0.43 ns

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was p< 0.05.
n=number of subjects; ns= Not significant.

Pulmonary artery systolic pressure before correction (Pre bypass) between two groups are shown in table-VII. Mean pulmonary artery systolic pressure before correction (Pre bypass) in group-1 was 57.35±10.08 and 59.65±8.64 in group-2. The mean difference of pulmonary artery systolic pressure before correction (Pre bypass) was statistically not significant between the two groups (p > 0.05).

Table-VII

Comparison of Pulmonary artery systolic pressure before correction (Pre bypass) between two groups

Variable	Group 1 (n=20)	Group 2) (n=20)	P value
Pulmonary artery systolic pressure before correction (Pre bypass)	Mean±SD 57.35±10.08	Mean±SD 59.65±8.64	0.44 ns

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was p< 0.05.
n=number of subjects; ns= Not significant.

Table-VIII compares pulmonary artery systolic pressure after correction (Post bypass) between two groups. Mean pulmonary artery systolic pressure after correc-tion (Post bypass) in group-1 was 45.35± 9.06 and in group-2 was 50 ±7.87. Reduction of pulmonary artery systolic pressure after correction(Post bypass) were occurred in both groups. But the mean difference of pulmonary artery systolic pre-ssure after correction (Post bypass) was statistically not significant between the two groups ($p > 0.05$).

Table-VIII

Comparison of pulmonary artery systolic pressure after correction (Post bypass) between two groups

Variable	Group 1 (n=20)	Group 2) (n=20)	P value
Pulmonary artery systolic pressure after correction (Post bypass)	Mean±SD 45.35± 9.06	Mean±SD 50 ±7.87	0.09 ns

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test.
Level of significance was $p< 0.05$.
n=number of subjects; ns= Not significant.

Comparison of pulmonary artery systolic pressure at 7th post operative day bet-ween two groups are shown in table-IX. Mean pulmonary artery systolic pressure at 7th post operative day in group-1 was 41.35± 8.61 and in group-2 was 46.65 ±7.67. It was observed that mean pulmonary artery systolic pressure at 7th post operative day was significantly different between two groups ($p< 0.05$).

Table-IX

Comparison of Pulmonary artery systolic pressure at 7th post operative day between two groups

Variable	Group 1 (n=20)	Group 2) (n=20)	P value
Pulmonary artery systolic pressure at 7th post ope-rative day	Mean±SD 41.35± 8.61	Mean±SD 46.65±7.67	0.04 s

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was $p< 0.05$.
n = number of subjects; s = significant

Table-X shows pulmonary artery systolic pressure at 1 month after operation in two groups. Mean pulmonary artery systolic pressure at 1 month after operation in group-1 was 34.35 ±7.35 and 39.75 ± 6.79 in group-2. Statistically significant difference was present in between two groups ($p < 0.05$).

Table-X

Comparison of Pulmonary artery systolic pressure at 1 month after operation between two groups

Variable	Group 1 (n=20)	Group 2) (n=20)	P value
Pulmonary artery systolic pressure at 1 month after operation	Mean±SD 34.35 ±7.35	Mean±SD 39.75±6.79	0.02 s

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was $p< 0.05$.
n = number of subjects; s = significant

Table-XI shows pulmonary artery systolic pressure at 3 month after operation in two study groups. Mean pulmonary artery systolic pressure at 3 month after opera-tion in group-1 was 23.9 ± 4.91 and in group-2 was 27.9 ± 5.16. The difference of pulmonary artery systolic pressure at 3 month after operation between two groups was statistically significant ($p < 0.05$).

Table-XII shows cardiopulmonary bypass time between two groups. The mean car-diopulmonary bypass time in group-1 was 76.74±20.97 and in group-2 was 93.16 ±27.18. The mean difference of cardiopulmonary bypass time between two groups was statistically significant ($p<0.05$).

Table-XI

Comparison of Pulmonary artery systolic pressure at 3 month after operation between two groups

Variable	Group 1 (n=20)	Group 2) (n=20)	P value
Pulmonary artery systolic pressure at 3 month after operation	Mean±SD 23.9±4.91	Mean±SD 27.9±5.16	0.02s

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was $p< 0.05$.
n = number of subjects; s = significant

Table-XII

Comparison of cardiopulmonary bypass time between two groups

Variable	Group 1 (n=20)	Group 2) (n=20)	P value
Cardio pulmonary bypass time (Minute)	Mean±SD 76.74±20.97	Mean±SD 93.16±27.18	0.04 s

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was p< 0.05.
n = number of subjects; s = significant

Table-XIII compares mechanical ventilation time (Hours) between two study groups. Mean mechanical ventilation time (Hours) in group-1 was 10.75 ±7.27 and in group-2 was 15.9±8.21. It was observed that mean mechanical ventilation time (Hours) was significantly different between two groups (p< 0.05).

Table-XIII

Comparison of mechanical ventilation time (Hours) between two groups

Variable	Group 1 (n=20)	Group 2) (n=20)	P value
Mechanical ventilation time(Hours)	Mean±SD 10.75 ±7.27	Mean±SD 15.9±8.21	0.04 s

Data were expressed as Mean ± SD.
Statistical analysis were done by unpaired t-test. Level of significance was p< 0.05.
n = number of subjects; s = significant

Table- XIV demonstrates that there was no death in two groups.

Table-XIV

Comparison of death between two groups

Death	Group 1 (n=20)	Group 2) (n=20)	P value
Death up to discharge in post operative patients	0	0	
Death within 3 months after operation	0	0	

Discussion

The study was conducted in the department of cardiac surgery of Bangabandhu Sheikh Mujib Medical University and National Institute of Cardiovascular Diseases (*NICVD*) from February 2014 to February 2016 in left to right shunt atrial septal defect or ventricular septal defect or patent ductus arteriosus patients with moderate to severe pulmonary hypertension. Forty patients were selected for the study and were divided equally in group-1 and group-2. Twenty patients of group-1 received ambrisentan and another twenty patients of group-2 received sildenafil during preoperative and postoperative period. So far known that there was no available published data to compare between ambrisentan and sildenafil in pulmonary hyper-tension.

Sample size, duration of medication before surgery and variables for measuring surgical outcome of this study are consistent with the study conducted by Palma et al.[17] and Peiravian et al.[18] Moderate to severe pulmonary arterial hypertension patients were included in this study which was consistent with the study conducted by Palma et al.[17]

In Peiravian et al.[18], Palma et al.[17] and Midanya et al.[19] study reduction of mean pulmonary artery pressure occurred in patients receiving sildenafil. According to Galie et al.[20] and D'Alto et al.[21] mean pulmonary artery pressure significantly im-proved from baseline after 12 weeks in patients with pulmonary arterial hypertension receiving ambrisentan for 12 weeks. In this study pulmonary artery systolic pressure was reduced in both sildenafil and ambrisentan group. But more reduction of pul-monary artery systolic pressure was observed in ambrisentan group in comparison to sildenafil group at 7th post operative day, at 1 month after operation and at 3 month after operation in this study.

Palma et al.[17] found shortened cardiopulmonary bypass time and mechanical venti-lation time in a group receiving sildenafil preoperatively, peroperatively and post-operatively than the group receiving sildenafil from peroperatively. But in this study, cardiopulmonary bypass time and mechanical ventilation time was more short-ened in ambrisentan group than the sildenafil group.

Preoperatively cardiac catheterization was not performed in all cases. Colour Doppler echocardiography and direct intraoperative

measurements of pressure were the main-stays of estimation of pulmonary artery systolic pressure. Small sample size, lack of placebo group, purposively collection of samples, short observational duration are the limitations of the study.

For optimum dosing of ambrisentan and sildenafil in both paediatric and adult patients further study is needed. Large, multicentre, randomized, double-blind clinical trial with long-term follow-up is needed to validate the efficacy of ambrisentan and sildenafil in comparison with placebo or other vasodilators.

Conclusion:

Preoperative and postoperative therapy of ambrisentan had better surgical outcome than sildenafil in left to right shunt anomaly patients with moderate to severe pul-monary hypertension.

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ORIGINAL ARTICLE

Effects of Spirulina on Oxidative Stress in Patients with Stable Chronic Obstructive Pulmonary Disease (COPD)

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Abstract:

Background & objective: *Chronic obstructive pulmonary disease (COPD), is characterized by airflow limitation which is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases. Lungs are continuously exposed to oxidants and oxidative stress is associated with pulmonary airway narrowing due to enhanced inflammation. This study was designed to assess the effect of dietary supplementation of spirulina on oxidative stress in patients with stable Chronic Obstructive Pulmonary Disease.*

Patients & Methods: *This was a single-blind, randomized, prospective, placebo-controlled trial. Sixty COPD Patients were recruited from the indoor and outpatients department of National Institute of Diseases of Chest and Hospital (NIDCH), Mohakhali, Dhaka. Patients then subjected to randomize into 'Group-A' and 'Group-B'. Group-A was treated with spirulina and Group-B was given placebo in associations with conventional treatment.*

Results: *Spirulina intake for consecutive two months at 500 mg twice daily has significantly reduced serum content of MDA (pÂ0.05) and increased antioxidant parameters compared to their baseline levels (pÂ0.05 for GSH, Vit C level, activity of SOD and GST) while no difference occurred for lipid hydroperoxide and catalase (pÃ0.05). The magnitude of changes in MDA (pÂ0.05), GSH (pÂ0.05), GST (pÂ0.05), SOD(pÂ0.05) and Vit C (pÂ0.05) were all significantly greater in the Spirulina vs. the control group except lipid hydroperoxide (pÃ0.05) while significant decrease in catalase occurred in control group (pÂ0.05).*

Conclusion: *Spirulina reduces oxidative stress in COPD patients.*

Key words: *COPD, Spirulina, Oxidative stress.*

[Chest Heart Journal 2017; 41(2) : 102-108]

Introduction:

Chronic obstructive pulmonary disease (COPD), is defined as "a preventable and treatable disease with some significant extra pulmonary effects that may contribute to the severity in individual patients. The pulmonary component is characterized by airflow limitation which is usually progressive and associated with an

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abnormal inflammatory response of the lung to noxious particles or gases".[1]

Lungs are continuously exposed to oxidants, either generated endogenously by metabolic reactions or exogenously, such as air pollutants or cigarette smoke.[2] The lung has heavy reliance on superoxide dismutase (SOD) (EC 1.15.1.1), catalase (EC 1.11.1.6), and glutathione peroxidase (GSH-Px) (EC 1.11.1.9) as they are the major enzymatic antioxidants of the lungs.[3] Glutathione-S-transferase (GST) (EC 2.5.1.18), another antioxidant enzyme family, inactivates secondary metabolites, such as unsaturated aldehydes, epoxides, and hydroperoxides.[4] Vitamin C reduces oxidative stress and improves vascular function and structure.[5] Glutathione (GSH) provides antioxidant defenses by their ability to exist in reversible oxidized and reduced forms.[6] Reactive oxygen species are highly short lived and therefore the best way to estimate oxidative stress is to quantify the products of their reaction with lipids, proteins, and nucleic acids.[7] Thiobarbituric acid reactive substance measure is one such test which quantifies malondialdehyde (MDA), a product of lipid peroxidation.[7]

When the balance between oxidants and antioxidants shifts in favor of the former, from either an excess of oxidants and/or depletion of antioxidants, oxidative stress occurs.[8] *Spirulina* sp. (*Arthrospira* sp.) is a photosynthetic, filamentous nondifferentiated, spiral-shaped, multicellular, and blue-green microalgae that grows naturally in warm climates.[9] Spirulina contains several active ingredients, notably phycocyanin and ²-carotene that have potent antioxidant and anti-inflammatory activities.[10]

There is a current worldwide interest in finding new and safe antioxidants from natural sources such as plant material to prevent oxidative deterioration of food and to minimize oxidative damage to living cells.[11] The use of synthetic antioxidants has decreased due to their suspected activity as promoters of carcinogenesis as well as a general consumer rejection of synthetic food additives.[12]

Spirulina with its good content of antioxidant nutrients such as ²-carotene, vitamin E, selenium could possibly play a role in alleviating the pulmonary function abnormalities by scavenging endogenous and/or environmental oxidant sources.[13]

Patients & Methods:

This was a single-blind, randomized, prospective, placebo-controlled trial with initial screening of patients that included 4-weeks intensive investigation and management phase (run in period), followed by a baseline, monthly for 2 months follow-up phase to determine the serum level of Malondialdehyde (MDA), Lipid hydroperoxide, catalase, Superoxide Dismutase (SOD), Glutathione-S-transferase (GST), Glutathione (GSH) and Vitamin C of stage-III COPD patients.

The study was carried out in the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during April 2014 to March 2015. Samples were collected from both indoor and outpatients department (OPD). Spirometry was performed in respiratory laboratory of NIDCH and serum oxidative stress markers Malondialdehyde (MDA), Lipid hydroperoxide, catalase, Superoxide Dismutase (SOD), Glutathione-S-transferase (GST), Glutathione (GSH), Vitamin C were measured in the Department of Biochemistry of Dhaka University.

60 patients with COPD (defined by specific criteria) were reviewed and if inclusion and exclusion criteria fulfilled, written consent was taken and were registered for the study and data were collected.

Each case was included in this study by purposive sampling method. Sample patients were divided in to two groups by simple randomization.

- One group was given Cap.Spirulina 500 mg twice daily for oral intake after breakfast and after dinner in addition of their standard management (Inhaled Tiotropium- 18 mic.gm, Salmeterol- 50 mic.gm and Fluticasone- 500mic.gm, Tablet Theophylline 400 mg) for consecutive 60 days. (Group-A)
- Another group was given placebo in addition of their standard management (Inhaled Tiotropium- 18 mic.gm, Salmeterol- 50 mic.gm and Fluticasone- 500mic.gm,Tablet Theophylline 400 mg) for consecutive 60 days. (Group-B)

A well structured questionnaire was administered among the patients. Changes in symptomatology (by CAT score), spirometry result, serum oxidative stress enzyme, oxidant and antioxidant level were recorded in specific format.

Data analysis :

All the data were recorded systematically. Collected data were compiled and tabulated on a master sheet. Data was analyzed by using SPSS version 19 and was expressed as Mean ± SD. Appropriate test (Chi-square and both paired and unpaired t' test) was applied to find the significance of difference. Level of significance was set at p-value dd0.05.

Result:

A total number of 60 samples were collected from both inpatient department and outpatient department of Respiratory medicine at National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka. Among them 21 patients in group-A and 20 patients in group-B came to final follow-up. Serum level of MDA, Lipid hydroperoxide, catalase, SOD, GST, GSH, Vitamin C level were performed in each case at the beginning and monthly for consecutive 2 months. In the study mean age 56.81 (± 9.19) years were in group-A and 57.66 (± 9.17) years were in group-B. Male were predominant, 27 (90%) were in group-A and 28 (93.3%) were in group-B. Male and female ratio was 11:1. Mean BMI in group A were 23.45 (±4.21) and 22.95 (±4.54) in group B. Majority 29 (96.66%) smoker in group A and 28 (93.33%) smoker in group B (p Ã 0.05) that was not statistically significant and results are shown in Table-I. Spirulina intake for consecutive two months at 500 mg twice daily has significantly reduced serum content of MDA (pÂ0.05) and increased antioxidant parameters compared to their baseline levels (pÂ0.05 for GSH, Vit C level, activity of SOD and GST) while no difference occurred for lipid hydroperoxide and catalase (pÃ0.05). The magnitude of changes in MDA (pÂ0.05), GSH (pÂ0.05), GST (pÂ0.05), SOD(pÂ0.05) and Vit C (pÂ0.05) were all significantly greater in the Spirulina vs. the control group except lipid hydroperoxide (pÃ0.05) while significant decrease in catalase occurred in control group (p<0.05)

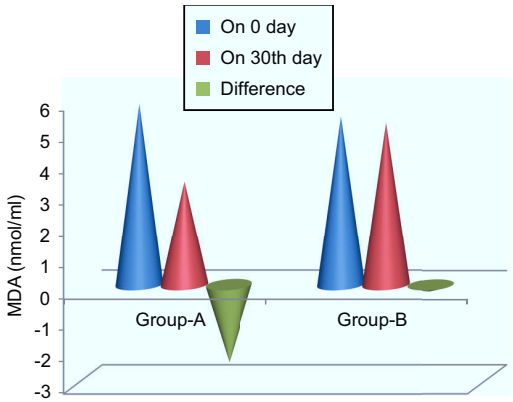
Table-I

Study population according to base line characteristics

Characteristics	Group-A (Case)	Group-B (Control)	P- value
Age in years (Mean±SD)	56.81 (± 9.19)	57.66 (± 9.17)	0.72
Gender			
Male (%)	27 (90%)	28 (93.3%)	0.55
Female (%)	03 (10%)	02 (6.7%)	
Smoking status			
Smoker (%)	29 (96.6%)	28 (93.33%)	0.65
Nonsmoker (%)	01 (3.4%)	02 (6.67%)	
BMI (Mean±SD)	23.45 (±4.21)	22.95 (±4.54)	0.89

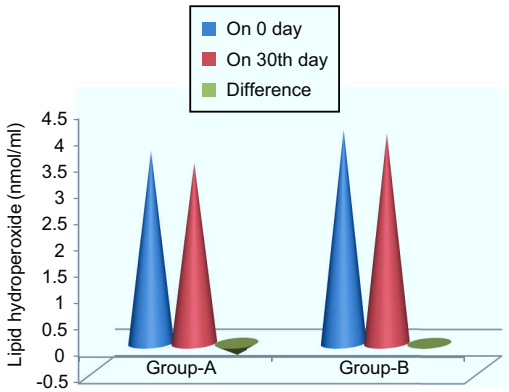
Group-A : Spirulina, Group-B : Placebo, p value reach from t-test and Chi square test.

Group-A: Spirulina Group-B: Placebo



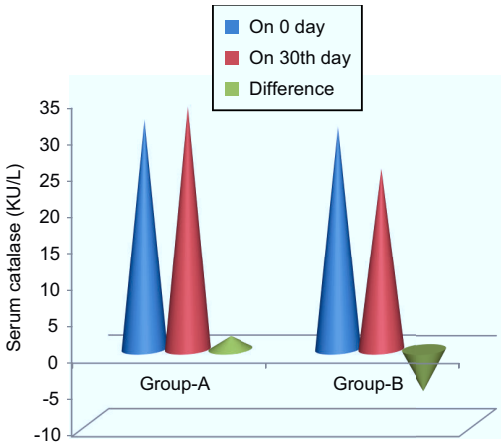
Group-A: Spirulina Group-B: Placebo

Fig.-1: *Serum MDA in two groups at the end of 30th day*



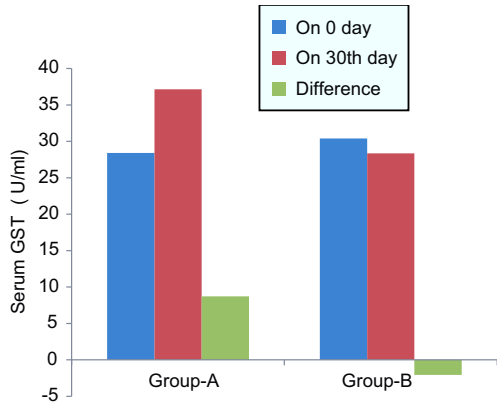
Group-A: Spirulina Group-B: Placebo

Fig.-2: *Serum lipid hydroperoxide in two groups at the end of 30th day*



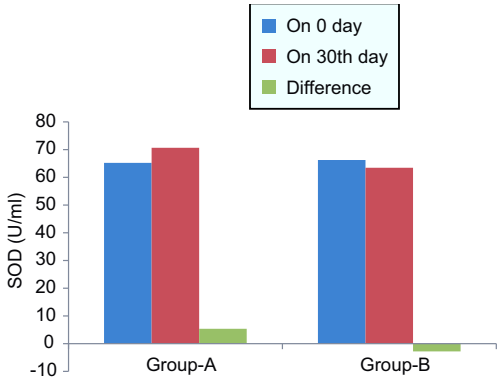
Group-A: Spirulina Group-B: Placebo

Fig.-3: *Serum catalase in two groups at end of 30th day*



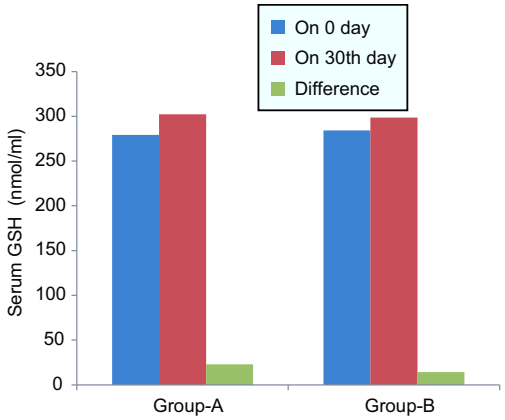
Group-A: Spirulina Group-B: Placebo

Fig.-5: *Serum gst in two groups at the end of 30th day.*



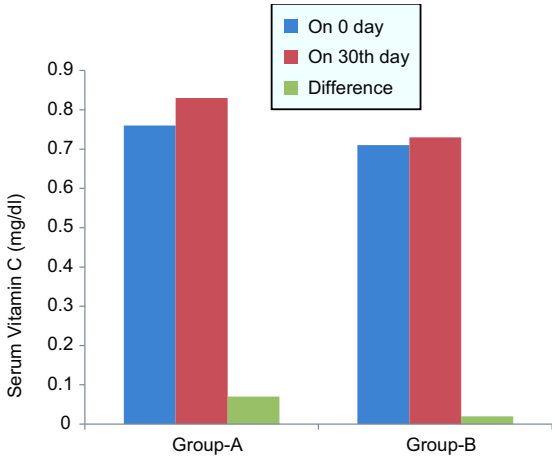
Group-A: Spirulina Group-B: Placebo

Fig.-4: *serum sod in two groups at the end of 30th day.*



Group-A: Spirulina Group-B: Placebo

Fig.-6: *serum glutathion (gsh) in two groups at end of 30th day*



Group-A: Spirulina Group-B: Placebo

Fig.-7: *serum vitamin c in two groups at the end of 30th day.*

Table-II

oxidative stress biomarkers in two groups at the end of 60th day

Oxidative stress biomarker	Group-A (Spirulina) n= 21 On 0 day Mean(±SD)	On 60th day Mean(±SD)	p-Value	Group-B (Placebo) n= 20 On 0 day Mean(±SD)	On 60th day Mean(±SD)	p-Value
MDA (nmol/ml)	5.58± 0.34	2.99±0.22	0.01s	5.78± 0.24	5.28± 0.27	0.28ns
Lipid Hydroperoxide (nmol/ml)	3.23±0.12	3.09±0.22	0.12ns	3.78±0.29	3.82±0.17	0.58ns
Catalase(kU/L)	28.53±7.42	30.05±8.08	0.33ns	31.03±8.41	24.83±5.37	0.03s
SOD(U/ml)	67.25±6.43	75.89±5.34	0.008s	65.21±8.43	60.15±7.63	0.07ns
GST (U/ml)	29.21±4.02	39.95±3.50	0.02s	28.41±4.02	25.35±3.82	0.41ns
GSH (nmol/ml)	281.32±21.24	332.61±13.61	0.01s	285.31±22.23	301.85±21.27	0.02s
Vitamin C (mg/dl)	0.78±0.07	0.92±0.05	0.02s	0.74±0.09	0.71±0.09	0.76ns

ns : not significant; S : significant; Malondialdehyde (MDA), Superoxide Dismutase (SOD), Glutathione-S-transferase (GST), Glutathione (GSH), Vitamin C

Table-III

Magnitude of changes in oxidative stress biomarkers in two Groups at the end of 60th day:

Parameter change	Group-A(Spirulina)	Group-B (Placebo)	p-Value
MDA (nmol/ml)	-2.59±0.25	-0.50±0.21	0.02^{s}
Lipid hydroperoxide (nmol/ml)	-0.14±0.17	0.04±0.21	0.66^{ns}
Catalase(kU/L)	1.52±4.70	-6.20±3.85	0.02^{s}
SOD(U/ml)	8.64±2.01	-5.06±2.65	0.03^{s}
GST (U/ml)	10.74±0.44	-3.06±0.25	0.01^{s}
GSH (nmol/ml)	51.30±5.04	16.54±4.35	0.01^{s}
Vitamin C (mg/dl)	0.44±0.02	-0.03±0.05	0.02^{s}

ns : not significant; S : significant; Malondialdehyde (MDA), Superoxide Dismutase (SOD), Glutathione-S-transferase (GST), Glutathione (GSH).

Discussion:

The inflammation in the respiratory tract of COPD patients appears to be a modification of the inflammatory response of the respiratory tract to chronic irritants such as cigarette smoke. The mechanisms for this amplified inflammation are not yet understood but may be genetically determined. Patients can clearly develop COPD without smoking, but the nature of the inflammatory response in these patients is unknown. Oxidative stress and an excess of proteases in the lung further modify lung inflammation. Together, these mechanisms lead to the characteristic pathological changes in COPD.[14]

Oxidative stress may be an important amplifying mechanism in COPD.[15] Oxidative stress not only produces direct injurious effects in the lungs, but also activates the molecular mechanisms that initiate lung inflammation and may have a role in many of the processes thought to be involved in the complex pathological events that result in COPD.[16]

The patients were predominantly male in the whole study population, male were predominant, 27 (90%) were in group-A and 28 (93.3%) were in group-B. Male and female ratio was 11:1 which indicate that the disease incidence was higher in male patients. Baseline and demographic

characteristics of the patients were similar between two groups.(pÃ 0.05)

No significant difference was observed between the groups regarding their base line oxidative stress biomarkers including MDA, lipid hydroperoxide, Vit C, GSH, SOD, GST,catalase (PÃ0.05). In the placebo group only serum GSH (p Â 0.05) concentrations was significantly increased by the end of first month and end of trial but catalase activity had significantly decreased (p Â 0.05). No difference occurred in placebo group for serum vit C, GST, SOD, lipid hydroperoxide and MDA (p Ã 0.05). In contrast, all assessed antioxidant parameters except catalase had remarkably increased in the spirulina group after first month and end of trial compared to their baseline levels (p Â 0.05 for vitC, GSH, SOD and GST). We found no difference in spirulina group for serum catalase and lipid hydroperoxide (p Ã 0.05) which differs from previous study.[17] The results of the present analysis clearly highlight the efficacy of spirulina as an MDA lowering agent. MDA levels were reduced in spirulina group by the end of first month and end of trial (pÂ0.05). This outcome is similar to the finding of another study.[18] The magnitude of changes in MDA (pÂ0.05), GSH (pÂ0.05), GST (pÂ0.05), SOD(pÂ0.05) and Vit C (pÂ0.05) were all significantly greater in the Spirulina vs. the control group except lipid hydroperoxide (pÃ0.05) while significant decrease in catalase occurred in control group (pÂ0.05) both in 30th and 60th day of trial. The above findings clearly in favour of ameliorating antioxidant status in COPD patients with spirulina supplementation. These findings are consistent with that reported in previous study.[19]

Conclusion:

COPD patients who received Spirulina as adjunctive therapy with conventional medication experienced improvement in serum antioxidant status.

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Department of Biochemistry, Dhaka University.

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ORIGINAL ARTICLE

Disease 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, 2016 to 30thJune, 2017. 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 hundreds and five (n=1305) patients were studied, of which 62% were male and 38% were female. Maximum patients (23.90%) belong to above 60 years of age. Maximum patients (69%) were come from outside Dhaka city and most of the studied patients were farmers (29.27%). Largest disease group was COPD (20.30%). Regarding disease pattern, 72.75% of patientspulmonary problem and rest 27.25 were non pulmonary problem. Among leading diseases, 20.30% were COPD, 15.86% bronchiectasis, 15.56% asthma, 13.41% postsurgical, 9.73% adhesive capsulitis, 8.58% cervical spondylosis, 6.90% low back pain 4.90% lung abscess, 4.75% others.

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

[Chest Heart Journal 2017; 41(2) : 109-112]

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 aûects 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 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

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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, 2016 to 30thJune, 2017. 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 1305. Among them 811 (62%) were male and 494(38%) were female. (Figure -1)

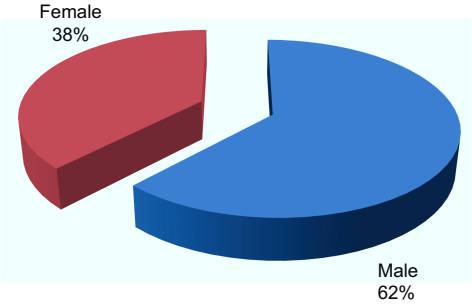

Fig.-1: *Sex distribution of the patients*

7.66% of patients were under 20 years of age, about 69% of patients belong to 2nd, 3rd, 4th, 5th decades. 23.90% were above 60 years of age (Figure -2).

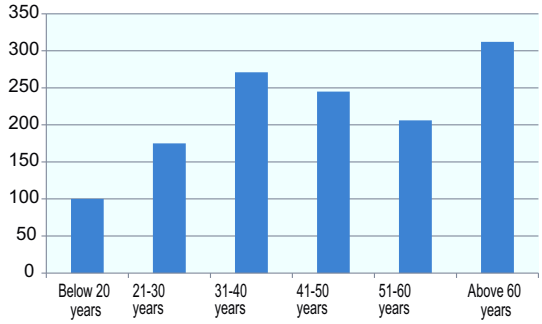

Fig.-2: *Age distribution of the patients*

69%of the patients were from outside the Dhaka city. Rest of the patients (31%) was from within Dhaka. (Figure -3)

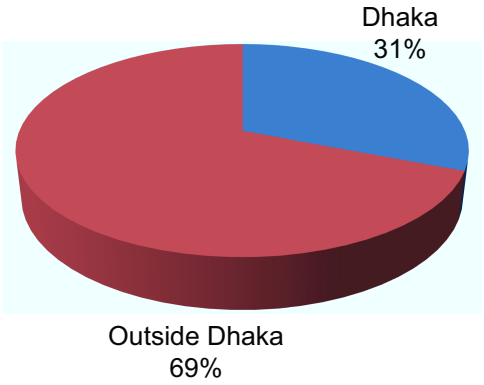

Fig.-3: *Catchment area of patients*

Among the total number of patients, majority(382) were Farmers (29.27%) followed by Housewives(26.67%), Labourer (15.86%), Service holder (10.57%), Businessman (9.35%) and Student(8.28%). (Figure -4)

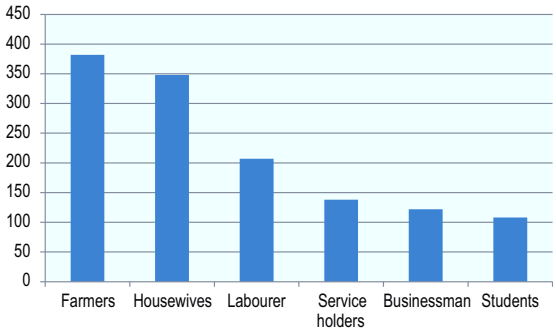

Fig.-4: *Occupation of the patients*

Among 1305 patients, 805 patients (61%)were from indoor and 504 patients (39%) were from outdoor. (Figure -5)

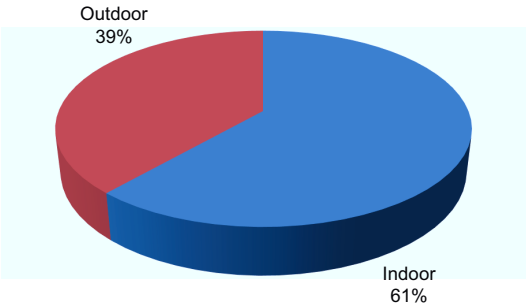

Fig.-5: *Indoor & outdoor patients*

Regarding disease pattern, 72.75% of patients were pulmonary problems and 27.25% were non pulmonary problem.Among leading diseases, 20.30% were COPD, 15.86% bronchiectasis, 15.56% asthma, 13.41% postsurgical, 9.73% adhesive capsulitis, 8.58% cervical spondylosis, 6.90% low back pain 4.90% lung abscess, 4.75% others. (Figure -6&Table-I)

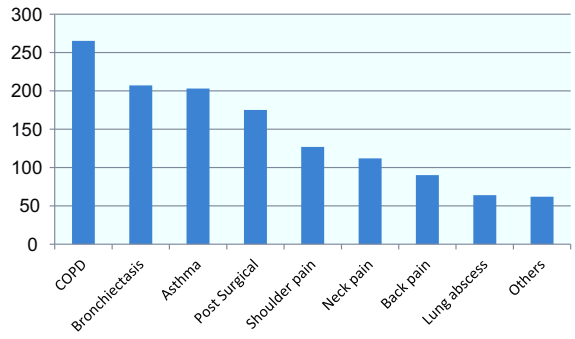

Fig.-6: *Disease proûle of the patients*

Table-I
Leading diseases

Disease	Number of patients	Percentage
COPD	265	20.30%
Bronchiectasis	207	15.86%
Asthma	203	15.56%
Post-surgical	175	13.41%
Adhesive capsulitis	127	9.73%
Cervical spondylosis	112	8.58%
Low back pain	90	6.90%
Lung abscess	64	4.90%
Others	62	4.75%

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, 62% of patients were male and 38% 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[4] showed that 52% were female and 42% were male. 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 wasfarmers (29.27%), Houseives (26.67), labourer (16.86%), serviceman (10.57%), businessman (9.35%) & student (8.28%).Hossain MS et al. found housewives (36.73%), farmer (15.56%), service holder (13.35%) in their study. MoinuddinM et al.[5] found housewives were 52.33% and Nessa J et al. were 37.3% housewife, 16.3% farmer,15.1% service holder in their studies.[7]

7.66% of patients were under 20 years of age, 13.41% were 21-30 years, 20.77% were 31-40 years, 18.77% were 41-50 years, 15.78% were 51-60 years and 23.90% were above 60 years of age. Hossain MS et al. showed most (27.96%) were between 41-50 years. MoinuddinM et al.[5] showed most (23.36%) were between 40-49 years, MoniruzzamanM et al.[6] also found 49.9% were in 41-50 years age.

In this study majority of patients had COPD-20.30%, bronchiectasis -15.86, asthma-15.56%, post surgical-13.41% & shoulder pain-9.73%.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 Shaheed Suhrawardy MCH7 and Moniruzzaman M at RpMCH[6] 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]

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.

Conclusion:

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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Chest Heart Journal
Vol. 41, No. 2, July 2017

ORIGINAL ARTICLE

Mammographic Evaluation of Mass Lesions of Breast, Correlation with Histopathological Findings

Jahan Afroze[1], Md. Wahiduzzaman Bhuiyan[2], Musavvir Samin[3]

Abstract:

Objective: *To evaluate the usefulness of Mammogram in the diagnosis and differentiation of mass lesion of Breast.*

Method: *This cross sectional study was carried out in the Department of Radiology and imaging, Dhaka Medical College Hospital during the period from July 2005 to 2007. Cases were collected from both surgery and gynaecology outdoors and indoors. Cases were also selected from BIRDEM, National institute of Cancer Research and Hospital, Dhaka in the same period.*

Result: *The peak incidence of breast malignancy was found to be in 4^{th} to 5^{th} decades comprising 41.67%. Out of 50 selected cases mammographically benign breast lesion were 39 (78%) and malignant breast lesions were 11(22%). 38 (76%) cases were diagnosed as benign breast diseases and 12 (24%) cases were diagnosed as malignant disease by histopathology. Mammographic abnormalities were found mostly in the upper and outer quadrant of the breast. In my study 1 found mammographic abnormality in 50 (100%) cases of which 12 (24%) were diagnosed as malignant. Among these 25 (50%) were in the upper and outer quadrant of breasts. Mass alone represents the most common abnormality. It comprises 37 (74%) of which 3 (8%) cases were malignant and 34(91%) were benign. The overall diagnostic accuracy of mammography was 90% and the sensitivity and specificity of positive diagnosis were 75%, and 94.74% respectively.* ***Conclusion:*** *The study concludes that mammography is the effective diagnostic tool and also an easier and reliable method for evaluation of mass lesions of breast non invasively.*

[Chest Heart Journal 2017; 41(2) : 113-118]

Introduction

In female, complex breast structure and extreme sensitivity to endocrine influences to a number of pathological conditions. Most disease of breast present as palpable lump, inflammatory lesions, nipple secretions, or mammographic abnormalities. There are several type of benign tumor, (non cancerous) & inflammatory lesion that at may develop with in different areas of the breast. For example ac chronic mastitis, fibrocystic diseases, fibroadenoma etc.[1] The term Breast cancer, refers to a malignant tumor that has developed from cells in the breast. Breast carcinoma is the most common cancer among women and is the second leading cause of cancer death among women between 40 & 55 years of age. Common forms of breast cancer are lobular carcinoma in situ, ductal carcinoma in situ, infiltrating ductal carcinoma. Less common forms of breast cancer are medullary carcinoma, mucinous carcinoma, tubular carcinoma, inflammatory breast cancer, Paget's disease of the nipple, phylloides tumor etc.[2]

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Breast cancer is most common cause of cancer death in women and overall fifth common cause of cancer deaths in the world.[3] Breast cancer most commonly occur in woman with a positive family history than general population (Russet, 2000).In Bangladesh remarkable increase of breast Cancer has occurred in the recent year. National Institute of Cancer Research showed cervical cancer ranked 1st & breast cancer ranked 2nd from 1996 to 2000. The management of patients with carcinoma breast can be improved if a definitive diagnosis is obtained preoperatively by Radiological Examination and/ or needle biopsy cytology. Early detection of breast cancer offers an important prospect of improving the out come of disease.[4]

Mammography is special type of x-ray imaging that uses low dose x-ray, high contrast, high resolution film, and an x-ray system designed specifically for mammography to create detailed images of the breast. Although breast x-rays have been performed since 1920s, modem mammography has only existed since about 1970. Modern mammography systems use extremely low-levels of radiation; usually about 0.1 to 0.2 rad dose per x-ray (rad is the scientific unit of measure of radiation energy dose).

A study in Bangladesh done by Mahmuda Begum et al.[5] has shown that clinical examination and mammography combined has a 90% sensitivity, 90%specificity and 97% accuracy in the diagnosis of malignant breast lump.

This study is designed to establish the mammography as a sensitive modality in the diagnosis and differentiation of mass lesions of breast by correlating the findings with histopathological examination.

Materials And Methods:

This cross sectional study was carried out in the Department of Radiology and imaging, Dhaka Medical College Hospital during the period from July 2014 to 2016. Cases were collected from both surgery and gynaecology outdoors and indoors. Cases were also selected from BIRDEM, National institute of Cancer Research and Hospital, Dhaka in the same period. All mammograms were done using the film screen technique and consisted of at least 2 views for each breast (craniocaudal and medio-lateral). Supplemental views were obtained when considered necessary for adequate visualization. By standard questionnaire case history, Mammographic findings and histopathology reports. All the collected data was compiled and tabulated on a master sheet. Further statistical analysis of the result was done by using computer software device with statistical package for social scientists (SPSS).

Results:

Table-I

Age distribution of the study subject

Age in	Malignant cases		Benign case	
years	No	%	No	%
31-40	3	25	33	86.84
41-50	5	41.67	5	13.16
51-60	4	33.33	0	00
Total	12	100	38	100

Table-II

Location of mammographic abnormalities

Breast location	Number o mammographic abnormalities	Percentage (%)
Upper & Outer Quadrant	25	50
Lower & Outer Quadrant	6	12
Upper & Inner Quadrant	6	12
Lower & Inner Quadrant	10	20
Retroareolar	3	6

Table-III

Histopathology proved diagnosis

Diagnosis	Number o mammographic abnormalities	Percentage (%)
Benign	38	76
Malignant	12	12

Table-IV

Mammographic & pathology correlation

Findings	Total number	Malignant	Benign
Mass only	37	3(8.11%)	34(91.89%)
Micro calcification	1	1(100%)	-
Asymmetric density	1	1(100%)	-
Mass with micro calcification with speculation	3	3(100%)	
Mass with speculation	3	3(100%)	
Mass with macrocalcification	4	-	4(100%)
Mass with enlarged axillary lymph node	1	1(100%)	-
Total	50	12	38

Table-V

Classification of patients based on test results

Mammography Test result	Histopathology True state of patient		Total Patients with positive
	True Positive	False Positive	
Positive (Malignant)	9	2	11
Negative (Benign)	3	36	39
Total	12	38	50

Sensitivity : 75%
Specificity : 94.74%
Accuracy : 90%
Positive predictive value : 81.80%
Negative predictive value : 92.31%1

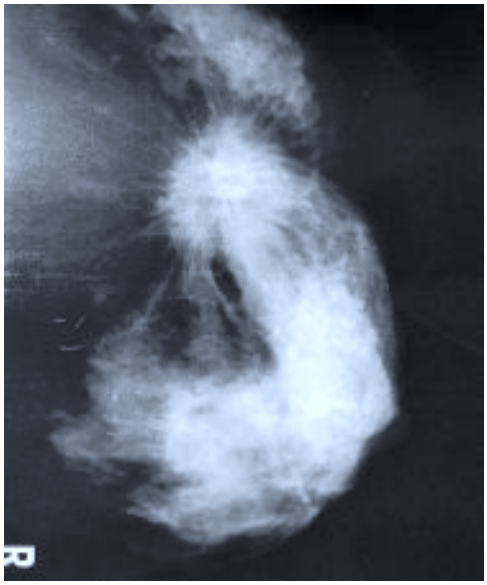

Fig.-1: *Invasive ductal carcinoma*

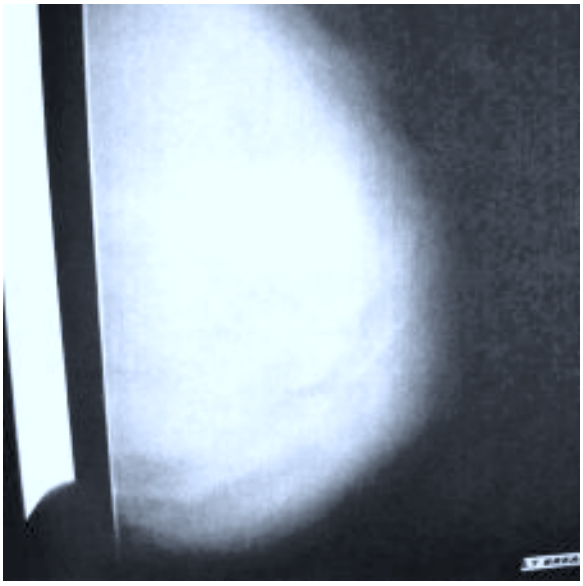

Fig.-2: *Galactocele*

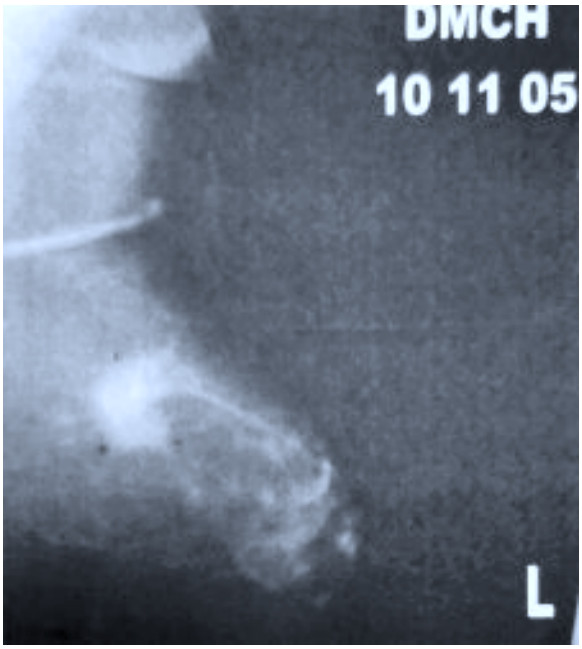

Fig.-3: *Infiltrating ductal carcinoma*

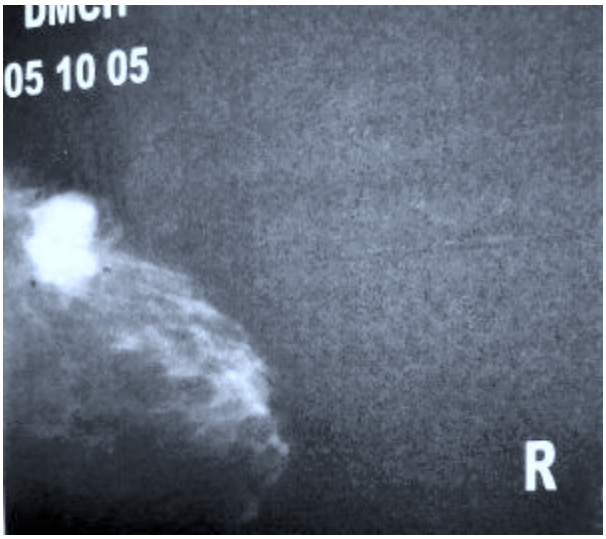

Fig.-4: *Infiltrating ductal carcinoma*

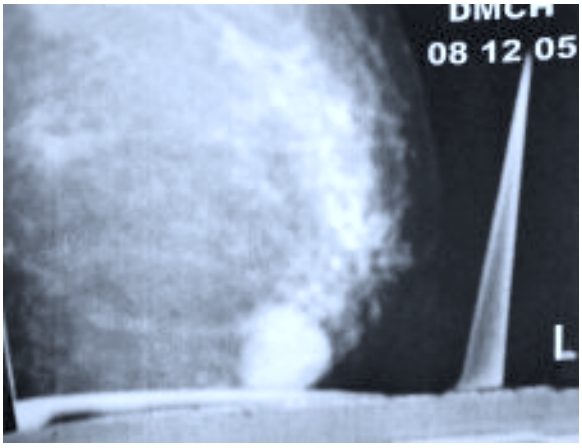

Fig.-5: *Fibroadenoma*

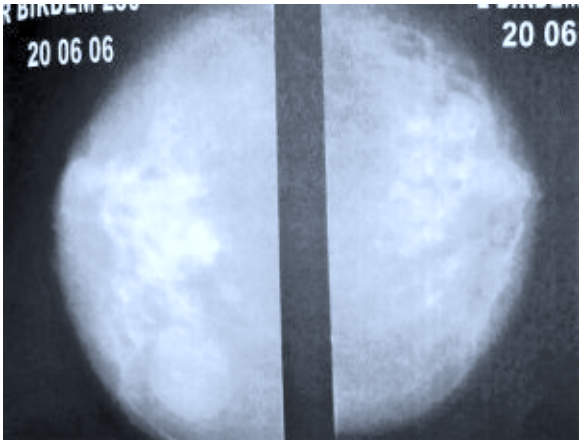

Fig.-6: *Fibrocystic changes*

Discussion:

Breast masses are common in female and amongst all the breast masses, malignant masses are the most feared.[6,7] Breast cancer is the commonest cause of cancer mortality in females[3] whereas breast cancer in men accounts for only 0.7% of all breast cancers.[8] The cross-sectional study was carried out to determine the diagnostic value of mammography and correlation with histopathology for the evaluation of mass lesion, the present study findings were discussed & compared with previously published relevant studies.

Initially seventy female patients with breast complaints with age ranging from thirty to sixty years were included in this study. Out of seventy patients of present study, eight patients refused to undergo mammogram. Sixty two patients underwent mammogram, but twelve patients refused to undergo surgical intervention. So these patients were excluded from this study because of no histopathological report. So the total number of the case was fifty.

Highest incidence of benign breast lesions was in between 31 to 40 years (86.84%) in this study

and the varieties were fibro adenoma and fibro cystic disease. Highest incidence of malignant mass lesion was 41 to 50 age group (41.67%) and was nil before age 30. another study was similarly described that common age incidence For breast carcinoma increases with age in the 4^{th} to 6^{th} decade.[9]

This study found 11 (22%) malignant cases mammographically and histopathologically proved cases were 12. Among these 12 malignant cases, 2 were non palpable. Out of 6 non palpable lesions, malignancy was found in 2 (33.33%) cases. The incidence of breast carcinoma among all non palpable mammographically detected lesion in this study fall within the 10 to 30 percent range, that most considered acceptable, if mammography is to be optimally reliable and cost effective.[10]

In this study it was found that mammogram was positive for 75% of the women and 25% women had false negative mammogram among malignant breast lesions. Another study reported that 78% women had positive mammogram and 22% women had false negative mammogram among 499 patients palpable carcinoma and were proven by biopsy.[11] This little dissimilarity of percentage of positive mammogram may be due to that, this study was done on a small group of patients (technical error).

In this study 3 malignancies were found in those masses interpreted as benign. According to Móskowitz mammographic masses are classified as highly suspicious, indeterminate, questionable or benign appearing. Also benign appearing masses over 1 cm in size had been reported as malignant in 2 to 6 percent of cases. Present study correlates with Meyer's work.[12]

It seems prudent to closely follow benign appearing masses (i.e. smooth borders, less than 1 cm) with repeat mammography and physical examination rather than indiscriminately biopsying all lesion.[10]

In the present series it was observed that malignant lumps were found more frequently in the left breast than in the right breast. Upper and outer quadrant of the breast was found frequently affected by the malignant tumor. Mahmuda Begum et al did the study on Role of Physical Examination of Breast and Mammography in the diagnosis of breast lump which was conducted in the Department of Radiology and Imaging, Dhaka Medical College, Dhaka. All cases underwent physical examination first and then mammography was done. At first physical examination of breast was performed by the researcher. Examination was also done by a specialist radiologist. Mammogram of both breasts was performed in MLO and CC projection as per standard technique. One radiologist interpreted mammogram separately without knowing the finding of clinical examination. One radiologist interpreted the mammogram after doing the physical examination himself. All information was gathered separately. Then all the patients underwent fine needle aspiration cytology. This method of examination and interpretation excluded any possibility of biasness and resulted in higher sensitivity than the present series.

In this study shows sensitivity of mammography in the present series is 75%. Sensitivity of mammography in the detection of breast cancer obtained by various authors ranges from 57% to 90%. The present series correlates with these works. Specificity for mammography ranges in the collected series from 90%-97%. Specificity of the present series is 94.74%. The overall diagnostic accuracy correlates well with other studies.[4,5,13,14]

Conclusion

Mammography is a valuable, useful, time relieving, non-invasive diagnostic tool in the early detection of breast carcinoma and in reducing mortality from this disease. We will get maximum benefit from mammography when applied rationally, with a thorough knowledge of both its limitations and significance of its many radiographic patterns and in conjunction with the relevant clinical perspective. Multiplicity of lump, calcification, architectural distortion, morphological characterization, lobulation and encapsulation are best seen in mammography. So, it can be used as mass screening both efficiently and inexpensively, to make it available and economically feasible for all women.

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Chest Heart Journal
Vol. 41, No. 2, July 2017

ORIGINAL ARTICLE

Off-pump Versus On-pump CABG: In Hospital Clinical Outcome

Subhash Ch. Mandal[1], Md. Shafiqul Islam[2], Saiful H. Talukder[3].

Abstract:

Throughout the world, as well as in Bangladesh, CABG operations are done in two procedures: conventional CABG (CCAB) and off-pump CABG (OPCAB). OPCAB surgery is being performed since 1997 in NICVD and then other cardiac centers in Bangladesh. But only one comparative study regarding clinical outcome between OPCAB and CCAB was performed in Bangladesh at NICVD, which was merely an initial experience of CABG on beating heart (Ahamed et al. 1988). So, a research work on this particular issue it strongly demanded to determine which technique we should adopt for better patient outcome .This is why we conducted a prospective observational study during the period of July/2014 to December/2016 to compare in-hospital clinical outcome of randomly selected patients divided into two groups: OPCAB and CCAB groups, each group having 60 patients with similar preoperative base line characteristics.

This study clearly demonstrated that OPCAB procedure is safe and is associated with some better short term clinical outcome in respect to CCAB procedure.

[Chest Heart Journal 2017; 41(2) : 119-123]

Definitions:

(i) Off-pump CABG (OPCAB): Coronary artery bypass graft (CABG) done on beating heart without cardiopulmonary bypass (CPB).

(ii) On-pump CABG i.e. conventional CABG (CCABG): Coronary artery bypass graft (CABG) done under CPB on cardioplegic arrested heart.

Introduction:

Coronary artery bypass grafting (CABG) is well established as the most effective operation for atherosclerotic coronary disease.

Before the era of cardiopulmonary bypass (CPB) (1950—1960), coronary endarterectomy and CABG were performed on beating heart[1]. But this early development was hindered by crude instrumentation, limited exposure and limited technical development and skill.

Since 1968, the widespread adoption of CPB and cardioplegia (CP) greatly facilitated coronary artery operations and then farther efforts to operate on beating heart have almost been forgotten[2]. Since then CABG under CPB has become the conventional method of myocardial revascularization.

Techniques of CPB have been refined for decades but some problems with CPB have been well documented.

To overcome the problems (morbidity and mortality) associated with CPB, renewed interest in CABG without CPB i.e., off-pump CABG (OPCAB) has raised lately and several series of CABG without CPB have been reported[3,4], showing better clinical outcome and cost effectiveness.

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Materials and method:

This was a prospective study carried out in the Department of Cardiovascular Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh during the period July, 2014 to December, 2016.

Patients scheduled for elective cardiac surgery requiring CABG operation were selected considering inclusion and exclusion criteria.

Data were collected from each participant using predesigned questionnaire and data collection form. The source of data was clinical information, hospital records and investigations.

A total number of 120 patients were studied. They were randomly selected. They were divided into two equal groups i.e. 60 patients in each group: off-pump group (subjected to OPCAB) and on-pump group (subjected to CCAB).

The patients of both groups were evaluated using specific evaluation criteria. These criteria were listed in (i) Demographic and preoperative variables, (ii) Per operative and (iii) postoperative variables.

Data were analyzed using standard statistical method.

Results and observations:

Demographic and preoperative baseline characteristics, peroperative and postoperative variables for evaluation and comparison of clinical outcomes were demonstrated in the tables (i) to (ix).

Table-I

Age distribution of the patients between the groups

Age of the patients (yrs.)	GROUP		p-value
	Off-pump CABG	On-pump CABG	
Mean age (yrs.)	50.15 ± 1.49	51.30± 1.33	0.972

Any p-value ,0.05 was considered significant. (Student's t-test).

Table-II

Sex distribution of the patients between the groups.

sex	GROUP		P-values
	Off-pump	On-pump	
Male	56(93%)	57(95%)	0.500
Female	4(7.0%)	3(5.0%)	

Any p-value <0.05 was considered significant. (Fisher's exact test).

Table-III

Distribution of NYHA functional class.

NYHA CLASS	Group		p-value
		On-pump CABG	
Class I	4(6.0%)	3(5.0%)	0.949
Class II	30 (50.0%)	27 (45.0%)	
Class III	26(44.0%)	30 (50.0%)	

Any p-value <0.05 was considered significant. (Chi-square test).

Table-IV

Comparison of risk factors between the groups

Risk factors	Group				p-values
	Off-pump CABG		On-pump CABG		
	Yes	No	Yes	No	
Current smoking	36(60%)	24(40%)	33(55%)	27(45%)	0.500
Diabetes mellitus	24(40%)	36(60%)	21(35%)	39(65%)	0.500
Hypertension	24(40%)	36(60%)	21(35%)	39(65%)	0.500
Hyperlipidaemia	15(25%)	45(75%)	9(15%)	51(85%)	0.347
Family history of CAD	(15%)	51(85%)	12(20%)	48(80%)	0.500

Any p-value <0.05 was considered significant.(Chi-square test).

Table-V

Comparison of number of coronary artery involved

No. of coronary arteries	Group		p-value
	Off-pump CABG (n=60)	On-pump CAB (n=60)	
Double vessel	30(50%)	36(60%)	
Tripple vessel	30(50%)	24(40%)	

Table-VI

Comparison of preoperative cardiac and pulmonary functional status:

Cardiopulmonary functional status	Group		p-value
	Off-pump CABG	On-pump CABG	
Ventricular Ejection Fraction (%)(Mean ± SEM)	54.2± 1.59	55± 1.42	0.678
FVC(L)Mean ± SEM)	2.96 ± 0.09	3.07 ± 0.11	0.461
FEV_1	2.48 ± 0.09	2.70 ± 0.07	0.049[s]

S=significant; any p-value Â0.05 was considered significant. (Mann Whitney test).

Table-VII

Comparison of peroperative variables between groups

preoperative variables	Groups		P-values
	Off-pump CABG	On-pump CABG	
Total operative time (hours)(Mean ± SD)	5.1 ± 0.51	5.6 ± 0.59	0.005[s]
No. of distal anastomosis (Mean ± SD)	2.50 ± 0.11	3.10 ± 0.23	0.081
Amount of blood loss (units) (Mean ± SD)	2.0 ± 0.16	2.9 ± 0.16	0.001[s]

S=significant; any p-value Â0.05 was considered significant. (Student's t-test and Mann Whitney test).

Table-VIII

Comparison of postoperative variables between groups

postoperative variables	Group		P-values
	Off-pump CABG	On-pump CABG	
Period of mechanical ventilation(hours) (Mean ± SEM)	7.55 ± 0.58	16.5 ± 0.45	Â 0.001s
ICU-Stay(hours) (Mean ± SEM)	37.2 ± 8.62	68.2 ± 4.75	Â 0.001s
Total hospital stay(days) (Mean ± SEM)	9.25 ± 0.25	10.6 ± 0.33	0.001s
Amount of blood required at ICU (units) (Mean ± SEM)	1.5 ± 0.14	2.8 ± 0.32	Â 0.001s

S=significant; any p-value Â0.05 was considered significant. (Mann Whitney test).

Table-IX

Comparison of complications between groups

complications	Group	
	Off-pump CABG (n=60)	On-pump CABG (n=60)
Re-exploration for bleeding	00	5 (8%)
Pulmonary complications:		
Pulmonary oedema	00	2(3%)
Atelactasis	00	2(3%)
Pleural effusion	00	2(3%)

Discussion:

National Institute of Cardiovascular Diseases, Dhaka, Bangladesh, has been performing central role in the field of cardiac surgery countrywide. NICVD is one of the best referral hospitals for coronary artery bypass graft (CABG) operation. The first CABG (on-pump) surgery was done at NICVD, Bangladesh, in 1985. OPCAB is being performed since 1997 in NICVD[5,6] and subsequently in other cardiac centers in Bangladesh. From 1st July, 2014 to 31st December, 2016, a total of 275 CABG was performed of which 48 (17·45%) were performed off-pump rest 227 (82·55%) were performed under conventional method (CCAB) i.e. under cardiopulmonary bypass.

This study, carried out at NICVD, included a total of 120 patients divided into two groups – off-pump group and on-pump group having 60 patients in each group.

From the tables we can see that age, sex, NYHA functional class and common risk factor distribution for coronary artery disease are almost uniform in both OPCAB and CCAB groups.

As regards to the number of coronary artery involvement, either group included only double and triple vessel disease. Though the distribution of involved vessels was not uniform, the difference was not statistically significant.

Preoperative cardiopulmonary functional status was compared using ventricular ejection fraction (EF%), FVC, and FEV_1. Data analysis showed that none but FEV_1 was significantly better on OPCAB group compared to CCAB group.

It is now clear that preoperative patient characteristics were almost similar in the study groups. So, those features should have no significant influence on peroperative and postoperative clinical outcomes. These preoperative patient characteristics were comparable to the study series of Boyd et al., 1999[7].

Comparison of peroperative variables between groups demonstrates that total operative time in OPCAB group (5.1±0.51 hours) is significantly less than that of CCAB group (5.6±0.59 hours). The amount of blood requirement in OPCAB group (2.0±0.16 units) was significantly less than CCAB group of patients (2.9 ±0.16 units).

Several postoperative variables were compared between the groups. Mean (mean± SEM) ventilation period in off-pump group was 7.55 ±0.58 hours and that in on-pump group was 16.50 ±2.01 hours. Average ICU-stay period in OPCAB group 37.3 ±5.88 hours and that in CCAB group was 68.2±4.75 hours. Total postoperative stay in hospital averaged 9.25 ± .25 days in OPCAB group and 10.60 ±0.33 days in CCAB group respectively. The mean blood requirement in OPCAB group during the postoperative period was 1.5±0.14 units and that in CCAB group was 2.80 ± 0.32 units. That total transfusion requirement in OPCAB procedure is much less is supported by many studies[8,9].

Thus the mean period of mechanical ventilation, ICU-stay period, total postoperative stay in hospital and amount of blood required at ICU during postoperative period all were significantly greater in CCAB group as opposed to OPCAB group.

All these reflect definite clinical advantage associated with OPCAB group of patients over CCAB group of patients.

The distribution of postoperative complications between the study groups was compared using appropriate statistical tests (table ix). Postoperative complications were relatively less in OPCAB group, although not statistically significant. But this might be significant if larger sample would have been taken. Mortality was nil in either group of patients.

Conclusion: CABG operation is increasing in our country and it is the most effective operation for CAD .In our country this operation is being performed through CCAB (conventional) and OPCAB procedure. This study clearly demonstrates that OPCAB procedure is safe and is associated with some better short term clinical outcome in respect to CCAB procedure. Therefore, continuing use of OPCAB procedure for myocardial revascularization is clearly justified whenever feasible and all cardiac surgeons should develop skill in this procedure.

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ORIGINAL ARTICLE

Effectiveness of Omalizumab in severe asthma inadequately controlled with Standard Therapy

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Abstract

Background: *Omalizumab, a recombinant monoclonal anti-IgE antibody, has demonstrated efficacy in patients with moderate to severe persistent allergic asthma. Patients with severe persistent asthma despite GINA 2005 step 4 treatment are at risk for asthma-related morbidity and mortality. This study aimed to investigate the efficacy, safety and long term control of asthma after discontinuation of omalizumab. in a private Hospital.*

Methods: *This is a retrospective study carried out in a private Hospital from January 2010 to June 2016 for assessing the efficacy of omalizumab therapy over 4 months and 9 month and to see the changes in asthma medication, asthma control, frequency of exacerbations and hospitalization rate at baseline and after omalizumab discontinuation. Asthma patients (age 20- 60 years) not controlled GINA 2005 classification step 4 treatment were selected and given injection omalizumab and followed up and compare the result of baseline and after 9 month of drug therapy.*

Results: *31 patients were included in this studied for the effectiveness of omalizumab,, 20 female and 11 male, mean age 45.71±21 years. There were no major adverse events from the study. Omalizumab significantly reduced the rate of clinically asthma exacerbations from 31.8%to 17.2% (P<.001) and all asthma-related emergency visits. There was a reduction in asthma medication post omalizumab therapy. It also improve the AQLQ score from 4.5±1.7 to 5.9±76 (P value <.05) and ACT score 11.17±23 to 13.89±12 (P value <.001). So the results shows significant improvement.*

Conclusions: *Patients receiving omalizumab therapy for 4 months and above were found to reduce the use of many asthma medications and also found less asthma exacerbation, ER visits, and hospitalization, even after the discontinuation of omalizumab. This study support that omalizumab is effective in patients with moderate to severe asthma .*

Keywords: *Omalizumab, Asthma, Retrospective study.*

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Introduction:

Bronchial asthma is a chronic inflammatory disease of airway characterized by hyper-responsiveness of the trachea and bronchi to various stimuli manifested by widespread narrowing of the airways that changes in severity either spontaneously or as a result of therapy[1].

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The most recent revised global estimate of asthma suggests that as many as 334 million people have asthma, and that the burden of disability is high[2]. About 7 million people in Bangladesh are suffering from asthma[3]. The unique guideline for the management and prevention of asthma adopted by Global Initiative of Asthma (GINA). Majority of the allergic and non allergic asthma can be well controlled by ICS+ LABA combination with or without short course use of oral steroid[4]. Severe asthma is characterized by a difficulty to achieve disease control despite high-intensity treatment. Current estimates of the prevalence of severe asthma are between 5 and 10% of all asthma[5]. These group of patients remains uncontrol with standard step care management and needs frequent ER visit and hospitalization. Before the introduction of Omalizumab, moderate to severe cases of asthma, regardless of their allergic or non-allergic nature had been generally treated with corticosteroids and bronchodilators. GINA recently added Omalizumab as add-on therapy in step care management. Omalizumab received approval by the Food and Drug Administration (FDA) in 2003 for treating patients 12 years and older with moderate to severe allergic asthma.(6) It has also received approval in many other countries for treating patients 12 years and older with severe, persistent allergic asthma and available in our country since 2007.

Omalizumab is a recombinant humanized monoclonal antibody directed against IgE to inhibit the immune response to allergen exposure. This anti-IgE is directed against the binding site of IgE for the high-affinity receptor and as a result, prevents free-serum IgE from attaching to mast cells and other IgE receptor-expressing cells thus preventing IgE-mediated responses

From the initial studies in patients with mild allergic asthma, omalizumab demonstrated clinical effects with inhibition of allergen-induced lung function changes in both the early- and late-phase bronchoconstrictor responses[7,8]. In patients with moderate-severe allergic asthma, omalizumab reduced asthma exacerbations and corticosteroid requirements[9-11].

Perhaps the most dramatic effect, which was not foreseen at the time when the anti-IgE therapy was designed and which was discovered during the clinical trials, is that as the free IgE in patients is depleted by omalizumab, the FcåRI receptors on basophils, mast cells, and dendritic cells are gradually down-regulated with somewhat different kinetics, rendering those cells much less sensitive to the stimulation by allergens[12,13,14].

Methods:

Data sources

This is a retrospective data based study from the records of outpatient care in a private hospital in Dhaka Bangladesh. The data sheet includes basic demographics, diagnoses from specialist, details of the ER visit and hospitalization, detailed information on prescribed medications.

Study design

After diagnosis of asthma their severity was assessed before treatment. Patients who have poorly controlled asthma despite taking high-dose inhaled corticosteroids (ICSs) and long acting $\hat{a}_2$-agonists (LABAs) and GINA 2005 classification Step IV management were included. Baseline GINA classification 2005, the ACT scoring, and the AQLQ score, Serum IgE level and details of current medications were recorded .

Patients were councilled and oral consent taken for their management with injection Omalizumab as add-on therapy. All the patients were started on omalizumab injections every 4 weeks, regimen. It is administered by subcutaneous injections. Dose of omalizumab is calculated based on the patient's weight and baseline IgE serum level. The patients were followed up monthly but detailed assessment were done at week 16 after initiation of drug to decide whether they would continue with the treatment based on the scientific leaflet.

After the second detail visit occurred at week 16 the final visit occurred at week 36 and each time by completing a) the Juniper Asthma Quality of Life Questionnaire (AQLQ), b) the ACT scoring c) Changes of GINA classification. d) the number of exacerbations and specific use of health care services were recorded during the study and compared with the patient's history in the 12-month period before treatment. Another group of patients who were prescribed

omalizumab due to presence of their indication as add-on therapy but did not received injection because of different reasons were also followed up. The results were compared with baseline for any clinically meaningful improvement after treatment initiation. .

Result:

The data including age, gender, Smoking history, and economic condition, educational status were recorded. In the treatment population (TP) majority 22(70.96%) of patients were aged 40 to 60 years old and male female ratio was 5:3. 22 (70.96%) 0f patients were nonsmoker, only 9(29.03%) of patients were ex-smoker.

Table-2 showed the physiological parameters related to asthma severity assessment both in treatment population and intended to treatment population. IgE level, AQLQ scoring, GINA 2005 classification leveling, and ACT scoring done at baseline for both group values shown in this table.

Table-3 shows the parameters of poor control of asthma before starting Omalizumab in both groups that means treatment population(TP) and intended to treatment population . Here in combine 38(67.85%) patients have daily day time symptoms, 37(66.07%) patients have weekly nocturnal symptoms. Specialist visit were needed 38(67.85%) patients and 22 (39.28%) have acute exacerbation. 100% needed ICS+LABA along with leukotriene receptor antagonist .

At 16 weeks of treatment GINA classification was revised. From the above table GINA classification of asthma changed significantly, thus frequency of daytime and nocturnal symptoms and FEV1 recorded were also changed significantly.

At 16 weeks ACT score was recorded. The ACT Score shown in the table overall response to treatment was good as compared to group Intended to treatment .ACT score at baseline was 11.17±23 which changes to 13.27±11, which is statistically significant P<.001.

Asthma related QoL was assessed at 16 week using Juniper asthma related QoL mini questionnaire (mini AQLQ). A change of ≥ 0.5 on the 7 points AQLQ represents a clinically meaningful improvement in asthma related AQLQ.

During Omalizumab treatment asthma exacerbation was also recorded. Severe exacerbation was defined as ER visit or hospitalization >1 day with oral steroid >20mg/ day; Non severe exacerbation was defined as oral steroid > 20 mg/day without ER visit or hospitalization.

At 36 weeks reassessment 12 patients discontinue the treatment after 16 weeks and only 19 patients completed 36 weeks treatment. These 19 patients were reassessed for parameter shown in the table-5 and found improvement in the GINA classification, ACT scoring, AQLQ scoring and severe exacerbation. At the end of follow-up, there was a reduction in all asthma medications compared to baseline and before the discontinuation of omalizumab. The doses of LABA/ICS, OCS, and SAMA also decreased post omalizumab therapy. There was a reduction in severe exacerbations or hospitalizations from baseline: 1 year before index day (31.2 %, n =31) to follow-up before discontinuation (11.8 %, n=19, p <0.001).

Table-I

Baseline demographic variables (n=31)

Variables		TP-31	ITP-25	
Age	22- 40 yrs	6(19.35%)	5(20%)	Mean age 45.71±21
	41-60 yrs	22(70.96%)	17(68%)	
	>60 yrs	3(9.67%)	3(12%)	
Sex	Male	20(64.51%)	15(60%)	M: F= 5:3
	female	11(35.48%)	10(40%)	
weight	Mean body wt	57.9±21.2	56.2±21.1	
Smoking History	Current smoker	00	00	
	Ex-smoker	9(29.03%)	7(28%)	
	Non- smoker	22(70.96%)	18(72%)	
Economic condition		good	good	
Education		Higher	higher	

• (TP- Treatment population, ITP- Intended to treatment population.)

Table-II

Baseline Physiological variables

Variables	Range	TP (mean ±SD)	ITP (mean ±SD)
IgE	350 to >2000	763±14 IU/ml	740±1.06 IU/ml
FEVI(% pred)	43- 76	65.8±21	64.7±1.98
AQLQ	overall	4.5±1.7	4.5±1.6
	symptoms	4.6±1.4	4.6±1.1
	Activity limitation	5.1±1.3	4.9±1.8
	Emotion function	4.2±1.1	4.2±1.3
	Envn. stimulation	4.0±1.9	4.0±1.2
GINA classification	Step III — V	Step III-IV	Step III-IV
ACT score	19—8	11.17±23	11.13±15

•(IgE- Serum IgE level, FEV1- Force expiratory volume in first second, AQLQ- Asthma quality of life questionnaire, GINA- Global initiative for asthma, ACT- Asthma control test.)

Table-III

Indices of poor asthma control prior to Omalizumab

Variables	Frequency	TP-31	ITP-25	Total-56	%
Day time symptoms	< once/week	4	4	8	8(14.28%)
	>once/week	4	6	10	10(17.85%)
	Daily	23	15	38	38(67.85%)
Night times symptoms	<2 times/ month	3	3	6	6(10.7%)
	>2times/month	6	7	13	13(23.21%)
	weekly	22	15	37	37(66.07%)
Asthma health care visit	ER visit e"1/ year	6	7	13	13(23.21%)
	Specialist visit e" 1/year	23	15	38	38(67.85%)
	Hospitalization e"1/year	2	3	5	5(8.92%)
Asthma exacerbation	≥1/year	13	9	22	22(39.28%)
concomitant Medication	ICS+LABA	31	25	56	56(100%)
	Oral steroid daily	5	4	9	9(16.07%)
	intermittent	26	21	47	47(83%)
	Leukotriene antagonist	31	25	56	56(100%)
	Anticholinergic	9	6	15	15(26.78%)
	Theophylline/derivatives	28	21	49	49(87.5%)

•(ER- Emergency room ,ICS+LABA- Inhale corticosteroid+ Long acting B2 agonist)

Table-IV

At 16-weeks Omalizumab treatment effectiveness

Population	N	baseline	16 wks effective	P value
% improving in GINA classification				
ITP	25	Step III-IV	Step III/IV	NS
TP	31	Step III-IV	Step III	S
% improving in ACT Scoring				
ITP	25	11.13±15	12.23±	NS
TP	31	11.17±23	13.27±11	P<.001
% improving in AQLQ score				
ITP	25	4.5±1.6	4.5±19	NS
TP	31	4.5±1.7	5.2±1.0	P<.05
Severe exacerbation free				
ITP	25	33.7%	31.9%	NS
TP	31	31.8%	19.5%	P<.001

• (TP- Treatment population, ITP- Intended to treatment population. NS- Not significant, S- significant)

Table-V

36-Weeks Omalizumab treatment effectiveness

Population	N	baseline	36 wks effective	P value
% improving in GINA classification				
ITP	25	Step III-IV	Step III/IV	NS
TP	19	Step III-IV	Step III	S
% improving in ACT scoring				
ITP	25	11.13±15	12.27±11	NS
TP	19	11.17±23	13.89±90	<.001
% improving in AQLQ score				
ITP	25	4.5±1.6	4.6±23	NS
TP	19	4.5±1.7	5.9±76	P<.05
Severe exacerbation free				
ITP	25	33.7%	31.9%	NS
TP	19	31.8%	17.2%	P<.001

• (TP- Treatment population, ITP- Intended to treatment population. NS- Not significant, S- significant)

Discussion:

This study was carried out from January 2010 to June 2016 in a private general hospital to see the effectiveness of Omalizumab in moderate to severe asthma patients. The standard step care management in some percentage of severe asthma is not sufficient for well control even with short course of oral steroid. So some other means should be employed to treat these patients. Omalizumab is costly and not widely available drug and should be given in injectable form only. In these regard the efficacy of the drug must be studied vigorously, which inspire us for the study. Here we can see that the majority of patients with severe asthma between the age group of 41-60 years (70.96%) with mean age 45.71±21 with M:F ratio 5:3 this result is consistent with other previous study. This study finding shows that the patients who received omalizumab therapy in a scheduled dose on the basis of serum IgE level and body weight for at least 16 weeks were found to have well asthma control in terms of reductions in asthma medications, exacerbation and related to other parameter even after discontinuation of drug.

Poorly controlled asthma patients with standard care therapy need repeated short course oral steroid and hospitalization due to exacerbation so this is an important parameter to see the effect of omalizuma. During Omalizumab treatment asthma exacerbation was also recorded. Severe exacerbation was defined as ER visit or hospitalization >1 day with oral steroid >20mg/day; Non severe exacerbation was defined as oral steroid > 20 mg/day without ER visit or hospitalization. In this study showed the significant reduction of exacerbation in Omalizumab group from31.8% to 17.2% (P value <.001) which was highly significant. This is important because patients are free from the side effect of steroid and relief from economic burden. The result of this parameter is consistent with that of Holgate et al.(15) and a more recent study from Ireland [16] who showed that the reduction of exacerbation from 3.48±2.20 to .93±0.83.

Asthma control test (ACT) is a brief patients based assessment tool for control status of asthma. It assess asthma control over the past 4 weeks in a quantifiable manner. It consists of 5 questions that provide both the Physicians and patients, a quick and easy way to assess the level of asthma control. This test has been used in this study to see the effect of Omalizumab. Score >25 means total control of athma, score between 2o to 24 indicates well control, 10 to 19 not well control and score < 9 indicates chances of exacerbation asthma control test (ACT) score [17]. Nygaard L et al. (18) used ACT to assess the clinical effect of Omalizumab in their study and they found that there is statistically significant increase in ACT srore of 5.1 points

[95% confidence interval (CI) 3.1-7.2, p=.0001]. Yang W H et al. (19) also shows similar result where they found that overall ACT score at baseline was12.9±4.49 and Omalizumab resulted in clinically meaningful changes from baseline(e" 3points). In our study there was significant improvement of ACT score from baseline 11.17±23 to 13.89±90 (P value <.001). This result is comparable to other study.

FEV1 is an important lung function parameter which is used to see the reversibility of airway and also for monitoring the treatment response. This has been taken as a vital parameter for the effectiveness for Omalizumab in this study. For the uncontrolled allergic asthma baseline FEV1 was taken and these were measured after 16 weeks and 36 weeks. Busse 2001, Soler 2001, Buhl 2002 et al.[20,21,22] showed the significant improvement of FEV1 with treatment of Omalizumab. In this study also we have found the changes in the FEVI from baseline to final follow up 65.8±21 to 70.34±54 which is highly significant statistically (P value <.05) Our study is compatible with the findings from these studies in other countries, and it is the first short scale study our country.

Uncontrolled bronchial asthma patients have lower AQLQ due to decreased emotion ,social and physical activity. AQLQ is an important parameter containing four domains consist of emotion, social, physical activity and environmental effect used in this study to see the effect of Omalizumab. Filling up and analyzing the Mini AQLQ questionnaire at baseline and after 16 weeks and 36 weeks were used to assess the changes. In this way an increase in overall scoree"0.5 points is significant improvement. In our study, improvements in AQLQ overall scores was clinically significant (≥1.4-points) in most of the patients compared with the ITP group. This result was comparable with the study done by Buhl et al.[22] and meta-analyses done by Chipps et al. and Niebauer et al.[23,24].

Omalizumab is given in subcutaneous route and the dose should be appropriately adjusted depending on Serum IgE and body weight because reducing the dose of omalizumab below that in the dosing table was not recommended, as the resulting increase in free IgE[22,24] would cause deterioration in asthma control[25] which is revealed in The INNOVATE study (INvestigation of Omalizumab in seVere Asthma TrEatment). In this study, patients treated with Omalizumab with at least 16 weeks duration, there were reductions in asthma medications, exacerbations and ER visits compared with baseline. Our study is compatible with the findings of cited different studies and it is the first short scale study our country. A larger study and longer follow-up period may be warranted in future.

Conclusions:

Poorly controlled moderate to severe allergic asthma patients are prone to persistent symptoms, exacerbation and impaired quality of life. They also account for frequent use of oral corticosteroid which is associated diverse side effect. Omalizumab , the anti-IgE antibody used to treat these uncontrolled patients shows significant effectiveness. So Omalizumab reduces exacerbation, decreased asthma symptoms and asthma related hospitalization and also improved asthma quality of life. Omalizumab offers a new therapeutic option that can reduce the clinical and social asthma related burden.

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ORIGINAL ARTICLE

Efficacy of Nebulized Hypertonic Saline with Adrenaline Versus Normal Saline with Adrenaline in Children with acute Bronchiolitis

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Abstract:

Background: *Bronchiolitis is the most common cause of lower respiratory tract illness in infancy, and hospital admission rates appear to be increasing both in developed and developing countries around the world. RSV is the principal pathogenic organism. Relieving symptoms is the main aim of management and there is no convincing evidence that any other form of therapy will reliably provide beneficial effects in infants with bronchiolitis. Bronchodilators like salbutamol, anti-cholinergic ipratropium bromide, adrenaline and saline nebulization have been used with varying results. Patients treated with nebulized adrenaline exhibited only short time benefit in case of acute bronchiolitis. But very few randomized control trials with nebulized adrenaline & hypertonic saline solution have so far been done and proven to be better in relieving symptoms and also decreasing hospital stay.*

Objective: *To compare the outcome of acute bronchiolitis treated with normal saline and hypertonic saline solution with adrenaline.*

Methodology: *Forty-eight infants and young children (2-24 months) hospitalized with bronchiolitis (runny nose followed by cough, breathing difficulty, chest indrawing and rhonchi on auscultation) were enrolled in the study. It was a single blind randomized control trial. The study was conducted in Pediatric Pulmonology unit of BSMMU from January 2007 to June 2008. Children were randomized into three groups: (1) group A 1.8% Sodium Chloride solution (2) group B 0.9% Sodium Chloride solution (control) and (3) group C 3.6% Sodium Chloride solution. Each patient received 0.1ml/kg Adrenaline mixed with either group of Sodium chloride solution. Each patient was treated with 3 doses of nebulization after admissions, 08 hours after admissions and 16 hours after admissions. Clinical severity score (wheeze, chest indrawing, respiratory rate) also recorded before and after medication. Outcome of therapy was evaluated by respiratory rate, clinical severity score and O2 saturation before and after therapy.*

Results: *Fever, running nose, respiratory rate, heart rate, chest indrawing and rhonchi were improved after 3rd dose of nebulization in all three groups and the improvement was higher in group C but no significant ($p>0.05$) difference was observed. However, cough, breathing difficulties, hypoxia (SaO2) and CS score were also improved after 3rd dose of nebulization in all three groups and the improvement was significantly($p<0.05$) higher in group C with compared to others two groups.*

Conclusion: *The present study concluded that nebulized normal saline with adrenaline and hypertonic saline with adrenaline were found effective in children with bronchiolitis. Nebulized hypertonic saline with adrenaline was found more effective than normal saline with adrenaline.*

Key Words: *Bronchiolitis,Normal Saline,Hypertonic saline,Adrenaline.*

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Introduction:

Bronchiolitis is the most common cause of lower respiratory tract illness in infancy and hospital admission rates appear to be increasing both in developed and developing countries around the world. More than 70.0% cases are due to respiratory syncytial virus (RSV), other pathogens are parainfluenza virus, adenovirus, rhinovirus, influenza virus and Mycoplasma pneumoniae[1].

Acute Bronchiolitis is characterized by bronchiolar obstruction due to mucosal oedema and accumulation of mucus and cellular debris.

There is no convincing evidence that any other form of therapy will reliably provide beneficial effects in infants with bronchiolitis. Therapies such as bronchodilators, corticosteroids, physiotherapy, palivizumab, ribavirin, antibiotics or anticholinergics have not demonstrated any measurable clinical effect.

Bronchodilators like salbutamol are often used in the treatment of bronchiolitis but rather than beneficial effect bronchodilator may cause harmful effect to the patients. It may be secondary to irritant effect or osmotic effect of nebulizing solution on the airways or bronchodilator may inhibit hypoxia induced pulmonary vaso-constriction resulting in increased intrapulmonary shunting and a decreased in oxygen saturation [2].

Recent evidence has suggested that adrenaline may offer some clinical benefit. Although different nebulized solutions such as Salbutamol, Ipratropium bromide and Adrenaline are being used, research and there by guidelines to date support nebulized Adrenaline as drug of choice[3]. Study shows L- Adrenaline (1:1000 soln. Adrenaline, 0.1ml/kg) are more effective than that of salbutamol in case acute bronchiolitis. Study reveal that Adrenaline is not only effective but also inexpensive and relatively safe alternative[4]. With comparison to salbutamol nebulized Adrenaline also showed promising results due its unique mechanism of action in infants with bronchiolitis. It can decongest mucosa with alpha adrenergic vasoconstriction and this may in addition lead to decreased systemic absorption resulting in less tachycardia than salbutamol.

But more recent studies simply substituting normal saline with hypertonic saline solution with adrenaline has shown promising results in case of bronchiolitis by improving clinical severity score and decreasing hospital stay[5].Recently relatively low concentration (<3.0%) hypertonic solution is designed to use in order to decrease the possible negative effect of a higher concentrations (>7.0%) on the cilliary beat frequency and thus hypertonic solution was used in conjunction adrenaline solution in order to avoid any possible bronchoconstriction effect for the treatment of acute bronchiolitis[6]. So, from recent observations and studies, it is expected that nebulized adrenaline with normal or hypertonic saline may act effectively for the treatment of acute bronchiolitis.

Materials and Method

A randomized controlled clinical trial was conducted in the Pulmonology Unit of Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University Dhaka from January 2007 to June 2008. To determine the sample size, the following formula is used;

$$n = \frac{10.51[(R+1) - p_2 (R^2+1)]}{p_2 (1-R)^2}$$

Each group the estimated sample size was 16, therefore 3X16=48 sample was collected.

Children up to 2 years of age, children having preceding/existing runny nose with cough, problem of Breathing difficulty (as perceived by the caregiver), lower chest in-drawing, rhonchi on auscultation were marked as inclusion criteria.

Child with atopic conditions (asthma, allergic rhinitis, allergic conjunctivitis, atopic eczema), history of similar previous attacks, children with congenital heart disease and tuberculosis, children with chronic lung disease were in exclusion criteria. Patients, admitted into Paediatric Pulmonology Department after applying inclusion and exclusion criteria, were enrolled in the study. Children's are randomized into three groups. (i) Group A: 1.8% Sodium Chloride solution,

(ii) Group B: 0.9% Sodium Chloride solution and (iii) Group C: 3.6% Sodium Chloride solution.

The protocol of the study was approved by the Ethical Committee, Department of Paediatrics.

A structured questionnaire was filled up through a face-to-face interview with the caregivers at the very outset. Detailed history was taken and through physical examination was done. The children were randomized into any of the three groups. The random number had the respective group of 1.8% Nacl (A), 0.9% Nacl (B) and 3.6% Nacl (C). Then as per random number table each patient was chronologically categorized without remainder approach. Thus, out of 48 each 16 patients with male 12 & female 04, in group A were nebulized with 1.8% saline plus adrenaline, 16 children with male 10 & female 06, nebulized with 0.9% saline plus adrenaline in group B and 16 children with male 09, female 07, in group C nebulized with 3.6% saline plus adrenaline. Each patient received 0.1 ml/kg Adrenaline mixed with the solution of a container (either 4.0ml of either normal saline or 1.8% NaCl solution or 3.6% NaCl solution) by air driven nebulizer with face mask, according to random table number. Total three doses were given.1st dose (7:00 A.M) was given to patients after admission, 2nd dose was (3:00 P.M) 8 hours after admission and 3rd dose was given 16 hours (11:00 P.M) after admission. $Sa0^2$ prior to therapy and 30 minutes after nebulization and also clinical severity score was evaluated simultaneously after 1st, 2nd and 3rd dose i.e. after admission, 08 hours and 16 hours of admission period. Parameters was measured and recorded before and after therapy as per clinical severity score [11]. Feeding was allowed as usual like breast feeding and other milk formula feeding which the baby was getting before hospitalization. IV fluid with 20% restriction was given when oral feeding was not possible because of severe respiratory distress. Routine investigations like Hb%, TWBC, differentials, chest X-ray were done.

Statistical analysis

As we had taken three groups of which group B i.e. 0.9% Naci solution was taken as control group. So, at first step we compared group A and group B, then at second step compared group B and group C and at third step group C and group A. All data were checked for consistency and correctness and scrutiny. Finally, all the filled-up questionnaires were collected. In uni-variate analysis, simple means and standard deviations and proportion were used. For comparison of the efficacy among the groups Chi square test, paired t-test and ANOVA test were done. p value <0.05, <0.001 and >.05 were considered as significant highly significant and not significant respectively. The data entry, data clean and data analysis were done in SPSS software.

Results:

Socio demographic profile age, weight, sibs, sex, residence area normal vaginal delivery, breastfeeding, atopy in family and smoking were matched in all three groups. The Clinical severity score included presence of wheezing, presence of retractions and respiratory rate and also oxygen saturation and heart rate were observed and explained with statistical analysis

Table I reveals that mean respiratory rate among all groups of children were almost similar before nebulization. Respiratory rate decreased after 3rd dose of nebulization in group A from 64.8±8.5/min to 45.6±7.9/min in group B from 63.1±7.1/min to 47.7±10.3/min and in group C from 62.3±5.2/min to 45.8±5.2/min and the decrement was higher in group C. The mean difference of respiratory rate was not statistically significant (p>0.05) in ANOVA test (Table I).

Average heart rate of the children at nebulization was 126. Heart rate increased after 3rd dose of nebulization in all three groups and the increment was higher in group C. The mean difference of heart rate was not statistically significant (p>0.05) in ANOVA test (Table II).

Chest indrawing was found in all three groups of children. After 3rd dose of nebulization chest indrawing declined in all three groups of children but higher in group C, however no significant difference was found in all three groups.

Breathing difficulties was present in all three groups of children. After 3rd dose of nebulization breathing difficulty was improved in all three group but improvement was significantly (p<0.05) higher group C compared other two groups.

Oxygen saturation increased after 3rd dose of nebulization in all three groups and the increases was higher in group C. The mean difference of hypoxia (SaO2) were statistically significant (p<0.05) in ANOVA test. The mean hypoxia (SaO_2) increased 3.8±1.7% in group A, 1.6±2.8% in group

B and 4.8±2.5% in group C after 3rd dose of nebulization and the increased was significantly ($p<0.05$) higher in group C (Table III).

CS score decline after 3rd dose of nebulization in all three groups and the declinement was higher in group C. The mean difference of CS score was statistically significant ($p<0.05$) in ANOVA test

The mean CS score was about 8 among all group of children. The mean CS score decrease (Table IV)2.0±1.3 in group A, 1.1±0.9 in group B and 3.1±1.2 in group C after 3rd dose of nebulization and the decreased was significantly ($p<0.05$) higher in group C.

Table-I

ANOVA table for respiratory rate at different times in three groups

	Sources	SS	df	MS	F value	p value
Before nebulization	Between groups	51.50	2	25.750	0.521	0.598
	Within groups	2225.75	45	49.461		
	Total	2277.25	47			
Dose 1	Between groups	14.54	2	7.271	0.111	0.895
	Within groups	2955.94	45	65.688		
	Total	2970.48	47			
Dose 2	Between groups	78.17	2	39.083	0.527	0.594
	Within groups	3334.81	45	74.107		
	Total	3412.98	47			
Dose 3	Between groups	43.17	2	21.583	0.330	0.721
	Within groups	2945.81	45	65.463		
	Total	2988.98	47			

Group A: 1.8% Sodium Chloride solution
Group B: 0.9% Sodium Chloride solution and
Group C: 3.6% Sodium Chloride solution

Table-II

ANOVA table for heart rate at different times in three groups

	Sources	SS	df	MS	F value	p value
Before nebulization	Between groups	153.38	2	76.688	0.363	0.698
	Within groups	9518.94	45	211.532		
	Total	9672.31	47			
Dose 1	Between groups	209.38	2	104.688	0.534	0.590
	Within groups	8815.88	45	195.908		
	Total	9025.25	47			
Dose 2	Between groups	520.29	2	260.146	1.560	0.221
	Within groups	7506.38	45	166.808		
	Total	8026.67	47			
Dose 3	Between groups	173.79	2	86.896	0.461	0.634
	Within groups	8482.69	45	188.504		
	Total	8656.48	47			

Group A: 1.8% Sodium Chloride solution
Group B: 0.9% Sodium Chloride solution and
Group C: 3.6% Sodium Chloride solution

Table-III

Mean Hypoxia (SaO_2) on base line and after 3rd dose in all groups

	Group A (n=16) Mean±SD	Group B(n=16) Mean±SD	Group C(n=16) Mean±SD
Hypoxia (SaO_2)			
Before nebulization	91.6±3.0	91.7±2.4	91.9±2.6
Dose 3	95.3±3.3	94.3±3.7	96.0±3.6
Pair difference	3.8±1.7	1.6±2.8	4.8±2.5
P value 0.001	0.001	0.001	

Table-IV

Mean CS score on baseline and after 3rd dose in all groups

	Group A (n=16) Mean±SD	Group B(n=16) Mean±SD	Group C(n=16) Mean±SD
CS score			
Before nebulization	8.2±0.8	8.3±0.7	8.0±0.8
Dose 3	6.3±1.3	7.1±0.8	4.9±0.7
pair difference	2.0±1.3	1.1±0.9	3.1±1.2
p value	0.001	0.001	0.001

Group A: 1.8% Sodium Chloride solution
Group B: 0.9% Sodium Chloride solution and
Group C: 3.6% Sodium Chloride solution

Discussion:

This randomize control trial provided the opportunity to examine the management of bronchiolitis with adrenaline and saline of different tonicity. This RCT suggest that children with bronchiolitis can get relief by increasing tonicity of normal saline and adrenaline solution by nebulized form. This was a single blind randomized control study done in Paediatric Pulmonology unit of BSMMU from January 2007 to June 2008.

In this study 50% in group A i.e. 08 out of 16, in group B also 08 out of 16 and in group C 10 out of 16 were exclusively breast-fed up to 5 months. 42 cases among all groups lived in urban area and only 9 cases lived in rural area. In group A 43.7% family members, in group B 31.2% and in group C 37.5% were smokers. Cough was found in all cases but after 3rd dose of nebulization 09 children out of 16 in group A, 14 out of 16 in group B and 07 out of 16 had suffered from cough. Existing running nose or history of running nose was found in about 44%, 44% and 31% of group A, group B and group C respectively and no significant difference was found in between groups. Rhonchi was present in 87.5%, 93.8% and 75% in Group A, Group B and Group C respectively after 3rd dose of nebulization and difference was not found significant among all groups.

Mean respiratory rate decreased significantly after 3rd dose of nebulization which was 45.6±7.9/ min in group A, 47.7±10.3/min in group B and 45.8±5.2/min in group C. The mean difference of respiratory rate was not statistically significant. After 3rd dose of nebulization chest indrawing was present in about 75% in group A, about 81% in group B and 69% in group C. However, no significant difference was found in between groups. Breathing difficulty was present in about 88% case in group A, again 94% case in group B and 69% case in group C. After 3rd dose, improvement was detected in all groups but significantly higher in group C. Oxygen saturation was also significantly improved after 3rd dose of nebulization. Mean oxygen saturation was 95.3±3.3% in group A, 94.3±3.7% in group B and 96.0±3.6% in group C after 3rd dose of nebulization. CS score had also significantly improved after 3rd dose of nebulization. The

mean CS score after 3rd dose of nebulization was 6.3±1.3, 7.1±0.8 and 4.9±0.7 in group A, group B and group C respectively. Mean heart rate increased significantly after 3rd dose of nebulization which were 135.6+12.3/min in group A, 132.8+14.8/min in group B and 137.4+14/min in group C. But after 3rd dose of nebulization, the difference of mean heart rate was not statistically significant in all three groups.

Comparing the study results with the body of research done in the past in this field, certain salient differences both on terms of methodology and results were emerged. Several of the earlier studies used changes in total pulmonary resistance (TPR) to measure clinical outcome[7,8] Yet, experience suggests that TPR may not necessarily reflect the clinical status. With the use of sympathomimetic drugs if there is any reduction in FRC (functional residual capacity), simultaneously with the amelioration in airway narrowing there may be no change in measured total resistance, despite an improvement in the child's initial condition. Therefore, the measured changes in TPR may not necessarily correlate with clinical benefits. The problem of objective PFT (Pulmonary Function Test) measurement in small children further limits the use of this modality [8]. Certain authors used sedation with chloral hydrate before recording PFT in children, but this itself may affect respiratory status. Therefore, in our study we used CS score and oxygen saturation to assess the respiratory functional status and degree of distress. This score is non-invasive, have low inter-observer variation[9].

In this study relatively, low concentration i.e. up to 3.6% saline was used in order to decrease the possible negative effects of higher concentrations. The safety of an even higher concentration of 7% hypertonic saline with beta-2 agonists in cystic fibrosis patients was also documented.[5,10] Hypertonic saline not backed up with beta-2 agonists may cause bronchoconstriction especially in asthmatic patients. No such detrimental effect occurred using adrenaline and hypertonic saline mixture in our study. This is in concordance with the excellent safety profile reported by[11].

The study could not reflect weather hospital stay was reduced after therapy but still revealed data gave some promising result in terms of decreasing respiratory rate, increasing oxygen saturation and also relieving symptoms for a longer period (>8 hours). More research with higher saline concentrations and more frequent inhalation of hypertonic saline is warranted to further clarify this potential treatment modality. This treatment has an excellent safety profile.

Conclusion:

The present study concluded that nebulized normal saline with adrenaline and hypertonic saline with adrenaline were found effective in children with bronchiolitis. Nebulized hypertonic saline with adrenaline was found more effective than normal saline with adrenaline. The study only included 48 patients. Larger number of cases and multicenter trial are needed for such study. This single blind study can't rule out the chance of biasness. We could not detect RSV antigen of any patient due to economical constraint. The patients were observed only for forty eight hours due to lack of resource. So along with relieving symptoms whether the hypertonic and adrenaline solution can cut short hospital stay or not, could not be revealed through this study.

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ORIGINAL ARTICLE

Phenotypic Characteristics of Asthma COPD Overlap Syndrome in Patients attended at a Tertiary Care Hospital in Dhaka City.

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Abstract:

Background: *Asthma-COPD overlap syndrome (ACOS) has been recently described by international guidelines. Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease in which the clinical presentation and prognosis vary according to the phenotype.* ***Methods:*** *To identify patients with ACOS, a cohort of well-characterized patients with COPD. Evaluated the presence of specific characteristics associated with asthma in this COPD cohort, divided into major criteria (bronchodilator test > 400 mL and 15% and past medical history of asthma) and minor criteria (blood eosinophils > 5%, IgE > 100 IU/mL, or two separate bronchodilator tests > 200 mL and 12%). ACOS defined by the presence of one major criterion or two minor criteria. Baseline characteristics, health status (COPD Assessment Test [CAT]), BMI, airflow obstruction, dyspnea, and exercise capacity (BODE) index, rate of exacerbations.* ***Results:*** *Regarding symptoms, sputum production was found 44(58.7%) in ACOS group and 58(55.2%) in non ACOS group. Dyspnea (mMRC scale > 2) was found 34(45.3%) in ACOS group and 50 (47.6%) in non ACOS group. Mean FEV_1 % predicted was found 62.3±17.8 % in ACOS group and 60.7±19.9 % in non ACOS group. Mean FVC % predicted was found 85.7±18.3 % and 86.7±22.5 % in ACOS group and non ACOS group respectively. Mean FEV_1/FVC was found 54.6±11.1 in ACOS group and 53.1±11.4 in non ACOS group. Majority 41(54.7%) had II mild stage in ACOS group and 50(47.6%) in non ACOS group. Majority 49(65.3%) patients had bode index 0-2 in ACOS group and 64(61.0%) in non ACOS group.* ***Conclusion:*** *Long-acting muscarinic antagonist was statistically significant between ACOS group and non ACOS group. Majority patients had bronchodilator reversibility in ACOS group. Serum IgE- Immunoglobulin E was found significantly higher in ACOS group than non ACOS group.*

Keywords: *Asthma, COPD, Overlap Syndrome.*

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Introduction:

Asthma-COPD overlap syndrome (ACOS) has been recently described by international guidelines. A stepwise approach to diagnosis using usual features of both diseases is recommended although its clinical application

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is difficult.[1] Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease in which the clinical presentation and prognosis vary according to the phenotype. In the last years, one of the phenotypes of COPD, that is recognized as the Asthma-COPD Overlap (ACO) has received increasing attention.[2]

In respiratory medicine, the term overlap syndrome has been applied both to the association between obstructive sleep apnoea and chronic obstructive pulmonary disease (COPD)[3] and to patients with features of both asthma and COPD (asthma–COPD overlap syndrome [ACOS]).[4,5] Features of both asthma and COPD are common in a significant proportion of adult and elderly patients who present with symptoms of a chronic airways disease. The precise proportion of patients with features of both diseases is highly variable, and prevalence rates between 15% and 55% have been reported depending on the diagnostic criteria applied.[6,7] Notably, concurrent doctor-diagnosed asthma and COPD has been reported in between 15% and 20% of patients.[8,9] Globally, the prevalence of ACOS reported varies greatly due to the different diagnostic criteria used. Different epidemiological studies in which ACOS is defined as patients with COPD diagnosed with asthma before the age of 40 described prevalences of 13% and 17%.[1,10] Using the same definition, a multicenter, cross-sectional, observational study carried out in Spain including 3125 patients with COPD in primary care and specialized centers reported a prevalence of ACO of 15.9%.[11] The prevalence of ACO was determined to be between 1.6 and 4.5% in the general adult population and between 15% and 25 % in the adult population with COPD. Most research of treatments for airways diseases has been restricted to patients who meet standard definitions of either chronic obstructive pulmonary disease (COPD) or asthma, yet to distinguish COPD from asthma in adult patients who have clinical features of both can be challenging. Treatment guidelines provide scant advice on how such patients should be managed. With increasing recognition that asthma and COPD are heterogeneous diseases, attention has been directed to the needs of a group of patients with what is now termed asthma–COPD overlap syndrome (ACOS), particularly in view of the high morbidity in this population.[12]

Materials and Methods:

To identify patients with ACOS, a cohort of well-characterized patients with COPD. COPD was defined by smoking history e”10 pack-years and a postbronchodilator FEV1/FVC < 0.7 after 400 μg of inhaled salbutamol. The main goal of the study is to perform a multidimensional evaluation of patients with COPD to better define its natural history and potential clinical phenotypes. The recruitment period was between August 01, 2017, and January 31, 2018. Shaheed Suhrawardy Medical College Hospital, Dhaka. Patients were divided in to two groups 75 were ACOS and 105 were non ACOS, patients are currently in the follow-up period, but data analyzed in the present study come from the baseline assessments. Demographic and clinical data, evaluated at baselaine included anthropometric data (age, sex, and BMI), previous history of doctor-diagnosed asthma and atopy, comorbidities (Charlson index), smoking history, dyspnea (modified Medical Research Council [mMRC] scale), exacerbations in the previous year, health status by the validated of the COPD Assessment Test (CAT) and Clinical COPD Questionnaire, anxiety and depression (hospital anxiety and depression [HAD] scale), pharmacologic treatments spirometry, exercise capacity (6-min walking distance [6MWD]), and BMI, airflow obstruction, dyspnea, and exercise capacity (BODE) index. All patients signed an informed and written consent form. Patient data were anonymized in a database with a hierarchical access control to guarantee secure information access.

Results:

A total of 180 patients were included, among them 75 patients were ACOS and 105 were non ACOS. The mean age was found 61.5±9.3 years in ACOS group and 63.4±8.9 years in no ACOS group. Female was found 11(14.7%) in ACOS group and 17(16.2%) in non ACOS group. Smoking pack per year was found 52.3±24.3 in ACOS group and 55.5±26.7 in non ACOS group. Active smoker was found 28 (37.3%) in ACOS group and 31(29.5%) in non ACOS group. Mean BMI was found 23.6±2.5 kg/m^2 in ACOS group

Table-I

Sociodemographic and Clinical Characteristics of the population, According to the fulfillment of ACOS criteria

Characteristics	ACOS (n=75)	Non ACOS (n=105)	Pvalue
Age (years)	61.5±9.3	63.4±8.9	0.16^{ns}
Sex (Female)	11 (14.7)	17(16.2%)	0.78^{ns}
Smoking pack (year)	52.3±24.3	55.5±26.7	0.41^{ns}
Active smoker	28 (37.3%)	31(29.5%)	0.62^{ns}
BMI (kg/m^2)	23.6±2.5	22.9±2.7	0.08^{ns}
Symptoms			
Sputum production	44 (58.7%)	58 (55.2%)	0.64^{ns}
Dyspnea (mMRC scale >2)	34 (45.3%)	50 (47.6%)	0.76^{ns}
Charlson index	1.24±1.47	1.28±1.55	0.86^{ns}
FEV_1 % predicted	62.3±17.8	60.7±19.9	0.57^{ns}
FVC % predicted	85.7±18.3	86.7±22.5	0.75^{ns}
FEV_1/FVC	54.6±11.1	53.1±11.4	0.38^{ns}
GOLD stage			
I Mild	13 (17.3%)	18 (17.1%)	0.70^{ns}
II Mild	41 (54.7%)	50 (47.6%)	
III Severe	15 (20.0%)	24 (22.9%)	
IV very severe	6 (8.0%)	13 (12.4%)	
Bode index	1.85±1.72	2.02±1.87	0.53^{ns}
0-2	49 (65.3%)	64 (61.0%)	0.09^{ns}
3-4	21 (28.0%)	22 (21.0%)	
5-6	3 (4.0%)	16 (15.2%)	
7-10	2 (2.7%)	3 (2.9%)	
Long-acting muscarinic antagonist	47 (62.7%)	80 (76.2%)	0.04^{s}
Long-acting ²-agonist	55 (73.3%)	78 (74.3%)	0.88^{ns}
Inhaled corticosteroids	47 (62.7%)	75 (71.4%)	0.21^{ns}
Theophylline	4 (5.3%)	11 (10.5%)	0.21^{ns}

ACOS-Asthma-COPD overlap syndrome, BMI-Body mass index, FEV_1=Forced expiratory volume$_1$, GOLD = Global Initiative for Chronic Obstructive Lung Disease FVC-Forced vital capacity; s=significant; ns=not significant; P value reached from unpaired and Chi square test.

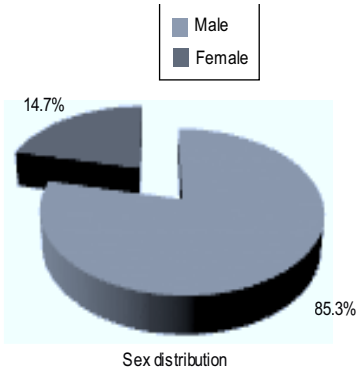

Fig.-1: *Sex distribution of ACOS patients*

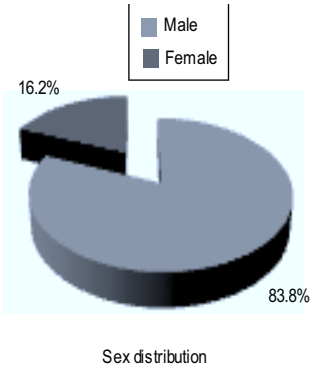

Fig.-2: *Sex distribution of Non ACOS patients*

and 22.9±2.7 kg/m^2 in non ACOS group (Table I). Regarding symptoms, sputum production was found 44(58.7%) in ACOS group and 58(55.2%) in non ACOS group. Dyspnea (mMRC scale > 2) was found 34(45.3%) in ACOS group and 50 (47.6%) in non ACOS group (Table I). Mean charlson index was found 1.24±1.47 in ACOS group and 1.28±1.55 in non ACOS group. Mean FEV_1 % predicted was found 62.3±17.8 % in ACOS group and 60.7±19.9 % in non ACOS group. Mean FVC % predicted was found 85.7±18.3 % and 86.7±22.5 % in ACOS group and non ACOS group respectively. Mean FEV_1/ FVC was found 54.6±11.1 in ACOS group and 53.1±11.4 in non ACOS group (Table I). Regarding GOLD stage, majority 41(54.7%) had II mild stage in ACOS group and 50(47.6%) in non ACOS group. Majority 49(65.3%) patients had body index 0-2 in ACOS group and 64(61.0%) in non ACOS group. Fourty seven (62.7%) patients had long-acting muscarinic antagonist in ACOS group and 80(76.2%) in non ACOS group. Fifty five (73.3%) patients had long acting ²-agonist in ACOS group and 78(74.3%) in non ACOS group. Fourty seven (62.7%) patients had inhaled corticosteroids in ACOS group and 75(71.4%) in non ACOS group. Four (5.3%) patients had theophylline in ACOS group and 11(10.5%) in non ACOS group (Table I). Long-acting muscarinic antagonist was statistically significant ($p<0.05$) between two groups (Table I). Majority 28(37.3%) patients had bronchodilator reversibility in ACOS group and majority 94(89.5%) patients had no bronchodilator reversibility in non ACOS group. Diagnosis of asthma was found 17(22.7%) in ACOS group and not found in non ACOS group. Fourty nine (65.3%) patients had IgE serum < 100 in ACOS group and 21(20.0%) in non ACOS group. Mean serum IgE was found 207.2±217 in

Table-II

Differential Characteristics of Patients with COPD Fulfilling the Criteria for ACOS

Characteristics	ACOS(n=75)	Non ACOS(n=105)	Pvalue
Bronchodilator reversibility			
No BDR	28 (37.3%)	94 (89.5%)	
Minor (>200 mL and >12%)	24 (32.0%)	11 (10.5%)	0.001^s
Major (>400 mL	and >15%)	23 (30.7%)	0 (0.0)
Diagnosis of asthma	17 (22.7%)	0 (0.0)	0.001^s
IgE serum >100	49 (65.3%)	21 (20.0%)	0.001^s
IgE serum	207.2±217	115.9±275	0.001^s
Eosinophils blood > 5%	25 (33.3%)	7 (6.7%)	0.001^s
Eosinophils blood >3%	39 (52.0%)	28 (26.7%)	0.001^s
Eosinophils blood	3.59±2.3	2.45±1.37	0.001^s
Chronic bronchitis	46 (61.3%)	62 (59.0%)	0.758^{ns}

IgE- Immunoglobulin E
s=significant; ns=not significant
P value reached from unpaired and Chi square test

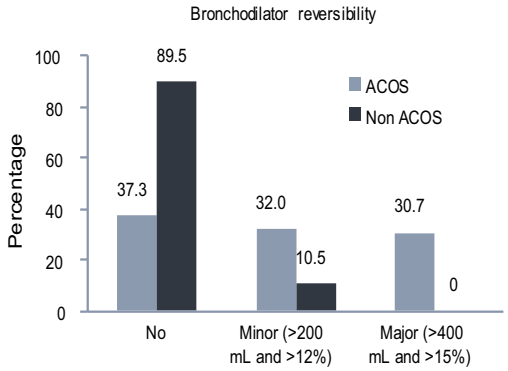

Fig.-3: *Bronchodilator reversibility of the patients.*

ACOS group and 115.9±275 in non ACOS group. Eosinophils blood > 5% was found 25(33.3%) in ACOS group and 7(6.7%) in non ACOS group. Eosinophils blood >3% was 39(52.0%) in ACOS group and 28(26.7%) in non ACOS group. Mean eosinophils blood was found 3.59±2.3 in ACOS group and 2.45±1.37 in non ACOS group. The difference were statistically significant ($p<0.05$) between two groups (Table II).

Discussion:

In present study observed that the mean age was found 61.5±9.3 years in ACOS group and 63.4±8.9 years in no ACOS group. Female was found 11(14.7%) in ACOS group and 17(16.2%) in non ACOS group. Smoking pack per year was found 52.3±24.3 in ACOS group and 55.5±26.7 in non ACOS group. Active smoker was found 28 (37.3%) in ACOS group and 31(29.5%) in non ACOS group. Mean BMI was found 23.6±2.5 kg/m^2 in ACOS group and 22.9±2.7 kg/m^2 in non ACOS group. Regarding symptoms, sputum production was found 44(58.7%) in ACOS group and 58(55.2%) in non ACOS group. Dyspnea (mMRC scale > 2) was found 34(45.3%) in ACOS group and 50 (47.6%) in non ACOS group. Mean charlson index was found 1.24±1.47 in ACOS group and 1.28±1.55 in non ACOS group. Mean FEV_1 % predicted was found 62.3±17.8 % in ACOS group and 60.7±19.9 % in non ACOS group. Mean FVC % predicted was found 85.7±18.3 % and 86.7±22.5 % in ACOS group and non ACOS group respectively. Mean FEV_1/FVC was found 54.6±11.1 in ACOS group and 53.1±11.4 in non ACOS group. Similar observation was found Baarnes et al.[13] mean age was found 63.0±10.5 years in COPD group and 56.2±11.7 years in non COPD group. Mean FEV_1 (% pred) was found 71.1±19.1 in COPD group and 92.5±17.5 in non COPD group. Regarding GOLD stage, majority 41(54.7%) had II mild stage in ACOS group and 50(47.6%) in non ACOS group. Majority 49(65.3%) patients had bode index 0-2 in ACOS group and 64(61.0%) in non ACOS group. Fourty seven (62.7%) patients had long-acting muscarinic antagonist in ACOS group and 80(76.2%) in non ACOS group. Fifty five (73.3%) patients had long acting ²-agonist in ACOS group and 78(74.3%) in non ACOS group. Fourty seven (62.7%) patients had inhaled corticosteroids in ACOS group and 75(71.4%) in non ACOS group. Four (5.3%) patients had teophylline in ACOS group and 11(10.5%) in non ACOS group. Long-acting muscarinic antagonist was statistically significant ($p<0.05$) between two groups.

In Sugimoto et al.[14] study reported that a total of 70 ACOS cases were identified. There were 58(83%) male patients, the mean age was 70.0±11.0 years. Sugimoto et al. study conducted a case-control study using 32 patients with ACOS exacerbations (ACO Sex) and 38 controls which had no exacerbations. Asthma severity was a significant risk factor for ACOS-ex. The age, sex, Body Mass Index, GOLD stage and smoking status adjusted odds ratio for moderate and severe persistent as compared with mild intermittent were 5.24(95% CI, 1.27-21.6, $p<0.05$) and 12.9 (95% CI, 1.10-149.9, $p<0.05$), respectively. de Marco et al.[15] study revealed that the subjects with current asthma alone were younger (mean±SD 33.6±7.2 years) and more likely to be women than subjects in the other groups (table 2), while subjects with COPD were the oldest (36.0±6.5 years). Smoking was more frequent among subjects with ACOS or COPD. Among lifetime smokers, the prevalence of heavy smoking (~*15 pack-years) was 51.5% for subjects with COPD alone (median (interquartile range) 16.8 (15.9) pack-years), and it ranged from 27.1% (healthy 9.8 (13.8) pack-years) to 35.1% (ACOS 10.3 (20.1) pack-years) in the other groups ($p<0.001$). In study of Cosio et al.[1] observed that Patients with ACOS defined by one major criteria or two minor criteria were not different by age (P=0.170) or sex (P=0.076) but there were significant differences by blood eosinophils (P <0.01) and IgE (P< 0.05). As expected from a population with COPD, patients were predominantly male, with predominantly mild to moderate disease assessed by lung function or BODE and with high prevalence of respiratory symptoms. Out of all comparisons, no statistically significant differences between patients with ACOS and those without ACOS were found, although there was a trend for higher disease severity in patients without ACOS (proportion of patients with BODE index e"5 was 6.7% vs 19.5%). Similarly, no differences in comorbidities were found between both groups, other than past diagnosis of asthma. The treatments that these patients were receiving

by the time of recruitment were similar for inhaled therapies in both groups, except for long-acting antimuscarinic agents (LAMAs) that were less frequently used in the ACOS group. Seventy-nine patients (63.2%) in the ACOS group were receiving inhaled corticosteroids. Oral theophylline was also prescribed significantly less frequently in the ACOS group (P < .05). In a sensitivity analysis, the significant differences observed when comparing ACOS to patients without ACOS in use of LAMA and theophylline were rendered non significant when stratifying by GOLD severity spirometry thresholds mild and moderate (I and II) vs severe and very severe (III and IV), with P values for LAMA 0.081 and 0.188, while 0.115 and 0.249 for theophylline.

In current study revealed that the majority 28(37.3%) patients had no bronchodilator reversibility in ACOS group and 94(89.5%) in non ACOS group. Diagnosis of asthma was found 17(22.7%) in ACOS group and not found in non ACOS group. Fourty nine (65.3%) patients had IgE serum < 100 in ACOS group and 21(20.0%) in non ACOS group. Mean serum IgE was found 207.2±217 in ACOS group and 115.9±275 in non ACOS group. Eosinophils blood > 5% was found 25(33.3%) in ACOS group and 7(6.7%) in non ACOS group. Eosinophils blood >3% was 39(52.0%) in ACOS group and 28(26.7%) in non ACOS group. Mean eosinophils blood was found 3.59±2.3 in ACOS group and 2.45±1.37 in non ACOS group. The difference were statistically significant (p<0.05) between two groups. Cosio et al.[1] study showed Fourty six (36.8%) patients had no bronchodilator reversibility in ACOS group and 633(89.7%) in non ACOS group. Diagnosis of asthma was found 28(31.2%) in ACOS group and not found in non ACOS group. Seventy (65.4%) patients had IgE serum < 100 in ACOS group and 88(19.8%) in non ACOS group. Mean serum IgE was found 206.6±232 in ACOS group and 115.7±273 in non ACOS group. Eosinophils blood > 5% was found 39(32.5%) in ACOS group and 34(5.2%) in non ACOS group. Eosinophils blood >3% was 61(50.8%) in ACOS group and 174(26.7%) in non ACOS group. Mean eosinophils blood was found 3.56±2.2 in ACOS group and 2.40±1.38 in non ACOS group. The difference were statistically significant (p<0.05) between two group. Following the proposed ACOS criteria, 66 patients would be diagnosed with ACOS by fulfilling one major criterion (28 patients with previous diagnosis of asthma and 39 with a bronchodilator response to albuterol higher than 15% or 400 mL) and 59 patients with two minor criteria. A Venn diagram with squares proportional to the weight of the major criteria in this population and with circles showing the overlap between minor criteria was built. In contrast, there is increasing awareness of the role of eosinophils in some types of patients with COPD, and blood eosinophilia has been identified as a surrogate marker of response to steroids in patients with COPD.[16]

Conclusion:

Long-acting muscarinic antagonist was statistically significant between ACOS group and non ACOS group. Majority patients had bronchodilator reversibility in ACOS group. Serum IgE- Immunoglobulin E was found significantly higher in ACOS group than non ACOS group. The study has been conducted on centre with a small sample size. So the study findings are not generalized in large scale and represent in whole country. Further large scale and multi centre study should be conducted to get the whole country scenario.

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CASE REPORT

Failed Coronary Angioplasty Successfully Treated with Coronary Endarterectomy: A Case Report

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Abstract:

Now-a-days, coronary artery disease patients getting more complex with multiple co-morbidities like hypertension, diabetes, renal impairment and also by failed PTCA. In this case report, a 56-year old male hypertensive and diabetic patient presented with occlusion in distal part of the right coronary artery, which was initially treated with balloon angioplasty at 6 months back. However, complete occlusion of stent in right coronary artery has occurred and also patient remains symptomatic in spite of aggressive medical management. After evaluation, complete myocardial revascularization done by coronary endarterectomy including removal of the stent from right coronary artery with coronary artery bypass graft surgery. A closed technique coronary endarterectomy was performed to remove the stents, and exhibiting the technical achievability of surgically re-moving occluded coronary stents. Postoperative period was uneventful and patient got discharged on 9th postoperative day. This case report demonstrates the safety and feasibility of coronary endarterectomy in the presence of an occluded stent in the coronary arteries.

Key words: Coronary endarterectomy, Coronary angioplasty, Coronary artery disease.

[Chest Heart Journal 2017; 41(2) : 145-149]

Introduction:

In the late 1957, Coronary endarterectomy was at first presented as a surgical option for myocardial revascularization by Bailey et al.[1] Coronary Endarterectomy (CE) is the expulsion of the atheromatous plaque, dismembering and isolating the outer media and adventitia layers and CE is frequently important to perform total myocardial revascularization during CABG or to encourage anastomosis of severely calcified and diffuse coronary arteries[1]. In spite of the presentation of coronary endarterectomy (CE) 60 year's prior as a strategy for treatment of diffuse coronary artery disease, its application

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remains controversial as it conveys a higher perioperative hazard and poor long term survival[1,2]. But complete myocardial revascularization for multi vessel CAD patients has been appeared to reduce the frequency of perioperative morbidity and mortality and the duration of hospital stay[3,4,5].

Case presentation:

A 56 years old ex-smoker, and diabetic male presented with dyslipidemia, hypertension and previous history of coronary angioplasty in right coronary artery. Patient also have had NYHA class III angina with a positive CAG (coronary angiogram) showed 60% stenosis in the mid part of left anterior descending coronary artery (LAD) and right coronary artery (RCA) was dominant with diffuse disease, a near total occlusion (100%) in the proximal and mid part of the RCA, just proximal to the stent and also poor retrograde blood filling from LAD circulation (Figure-1). During CAG a guidewire could not be inserted via RCA and also PTCA was not feasible to performed. Aggressive Medical management was started but patient remained symptomatic throughout the course of treatment. Due to his failed medical management and progressing stable angina, the patient went for elective coronary artery bypass graft (CABG) surgery with endarterectomy.

Standard intraoperative monitoring strategies were utilized and a CPB circuit was kept on standby for this cases. After standard median sternotomy, Heparin was used to maintain an ACT (Activated clotting time) more than 400 seconds just before dividing the harvested left internal mammary artery (LIMA). Operations was performed off pump CABG with CE (Coronary endarterectomy) and utilizing mechanical stabilizers like suction type and the compression type stabilizer to immobilize the target coronary artery during grafting. A conclusive decision to endarterectomize a vessel is made per-operatively and CE from RCA was considered in this patient because of localized complete lesion, and occlusion of stent with poor distal run-off.

Following coronary endarterectomy with removal of stent from RCA, a saphenous venous graft was performed to distal RCA with approximately 15mm incision over the stent. Left internal thoracic artery was used to graft LAD artery. The endarterectomy specimen was 11 cm long incorporated with the stent (Figure- 2) and little distortion of the stent was considered due to traction during the procedure. Histological examination of the atheroma specimen observed old thrombus occluding the lumen with fibrocartilage and macrophage (Figure- 3). The postoperative period was uneventful and patient got was discharged at 10th postoperative days. Patients was well at 6 month's follow-up and free of angina to date.

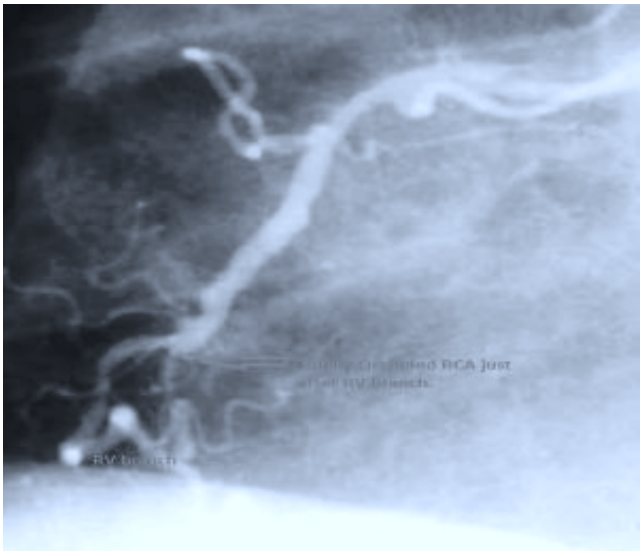

Fig.-1: *Coronary angiogram showed 100% stenosis at the proximal part of RCA just after RV branch with retrograde filling through left coronary circulation.*

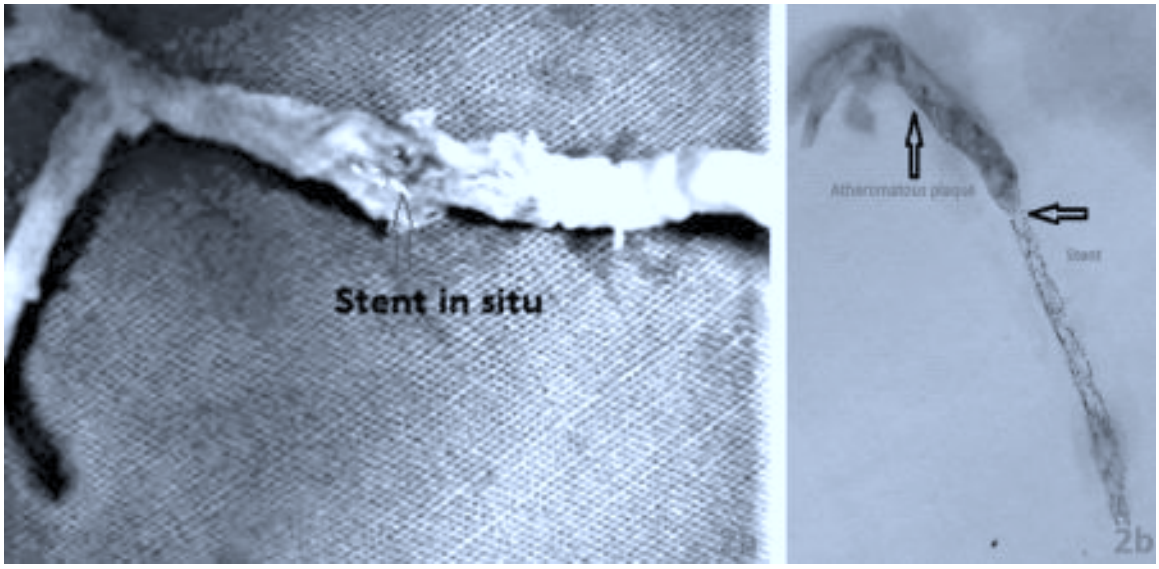

Fig.-2: *Post-operative specimen of atheroma and Stent. Distorted atheromatous plaque with stent in situ (2a); Stent with atheroma (2b).*

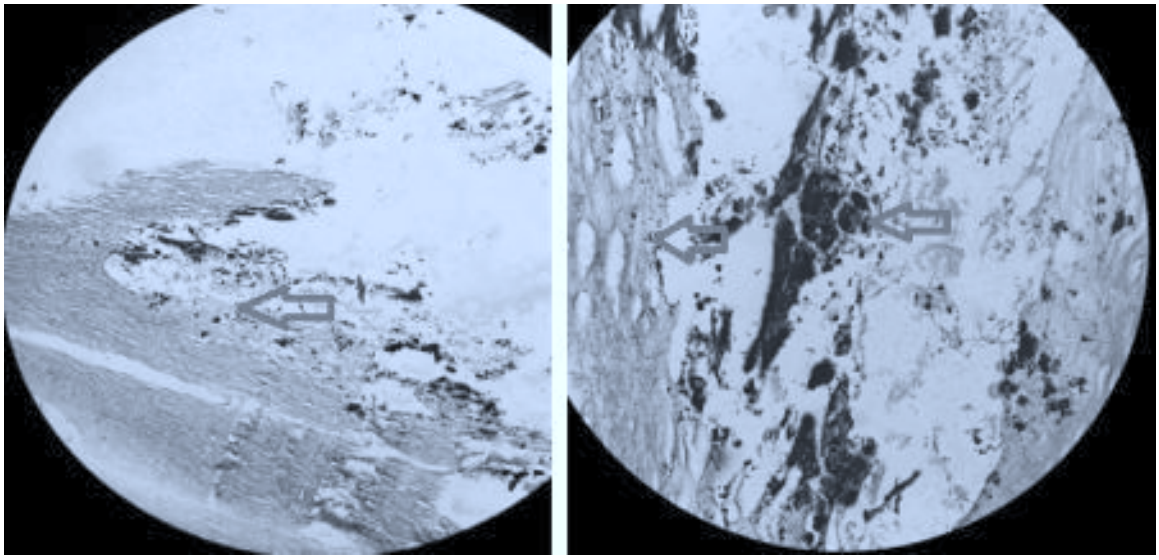

Fig.-3: *Histopathological study of atheromatous plaque revealed foci of calcification, hyaline cartilage and also fibrocartilage (arrow mark).*

Discussion:

In case of diffuse coronary artery disease, conventional CABG does not provide a satisfactory blood supply through the distal part of vessel, bringing about inadequate myocardial revascularisation[1]. Coronary endarterectomies were performed manually by slow sustain and continuous traction of atheromatous plaque with the aid of delicate Ring Forceps, utilizing the closed methods trailed by reproduction with anastomosis with pre-planned graft. The arteriotomy incision was roughly 8-10mm long, however that was stretched out for another 5mm in few cases, if complete removal of the plaque was not feasible[1,2,4,5]. In our study, arteriotomy incision was approximately 15cm; which is similar to other study.

In our case atheroma was 11 cm long; however, till date the reported longest atheroma was removed from RCA which was 14 cm in size in

Bangladesh described by Ranjan et al.[2] There are two techniques to perform coronary endarterectomy- Closed technique and Open technique. We utilized the closed "Traction technique- slow, sustain and continuous traction" to perform endarterectomy; which is also described by Ranjan et al. in their study[2,5-8]. But the potential dangers are inadequate expulsion of the plaque and the "snowplow effect," to be specific, shearing-off of the plaque in the side branches[6,9,10]. But with the "open procedure" the vision is better, and that may prompt more entire expulsion of the atheroma from the coronary vessel and its side branches. However, open technique is time consuming and required patch repair. So that, we preferred "traction technique" with careful examination of the atheromatous plaque after expulsion, which also supported by other articles also[2,7,8,10]. To ensure complete expulsion, the atheromatous plaque carefully inspected for a smooth distal tapper end. In addition, back flow of blood from the distal vessel following extraction of the atheroma is a consoling indication of adequate removal atheromatous plaque and that is special feature in OPCABG endarterectomy[11,12].

Anticoagulation therapy is very important in early postoperative period to prevent graft occlusion as well as native endarterectomized artery occlusion by thrombus[9,11]. Following coronary endarterectomy, routine Heparin infusion was prescribed to prevent thrombosis in the early post-operative period followed by oral Warfarin for next 6 months, and double anti-platelet agent for life long[2,5,10-14]. In our study, once postoperative blood draining is settle down (usually 3-4 hours following surgery), we started Heparin usually for 48 hours, followed by bridging to Warfarin (5mg) orally from 1st post-operative day. From 3rd Post-operative day, we started Warfarin (2.5-5mg) for next 6 months and dose adjusted according to INR findings (Targeted was INR 1.5-2.5). We also prescribed Clopidogrel and Aspirin (75mg) for life long following CE with OPCABG, which also described in other articles.[2,5,15]

This present case report observed that CE (Coronary endarterectomy) with off-pump coronary artery bypass graft is attainable and accomplishes total myocardial revascularization in presence of stent in coronary artery; when there are no other alternative options for sufficient revascularization.

Conclusion

Despite the higher risk group patients, surgical skill and the patient's selection criteria are main stream for better outcome following CE with CABG surgery in a patient with stent occlusion, and should not be considered a contraindication to surgical revascularization.

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CASE REPORT

Concomitant Esophageal and Pulmonary Neurofibroma Independent of Neurofibromatosis Type 1: A Rare Case Report

Manabendra Biswas[1], Mosharraf Hossain [2], Delwar Hossain [3], Asit Baran Adhikary [4], Md. Mushfiqur Rahman [5]

Abstract

Concomitant occurrence of esophageal and pulmonary neurofibroma without neurofibromatosis type 1 is exceedingly rare. We are reporting such a case; a 25 year old woman was under evaluation for her painless progressive dysphagia within a short period with history of intermittent fever. Barium esophagogram and esophgaoscopy revealed narrowing of mid and part of lower thoracic esophagus. A CT scan of chest with oral contrast delineated sub-segmental consolidation at posterior basal segment of lower lobe of right lung as well as a long segment circumferential wall thickening in 82.2 mm length of thoracic esophagus extending upto16.4 cm proximal to gastroesophageal junction with proximal dilatation. Patient underwent surgical management and diagnosis was confirmed by histopathology. Patient was discharged home thereafter with marked symptomatic improvement.

Key Words: *Esophageal neurofibroma, Pulmonary neurofibroma.*

[Chest Heart Journal 2016; 41(1) : 150-153]

Introduction:

A neurofibroma is a benign tumour originating from nonmyelinating-type Schwann cells in nerve sheath in the peripheral nervous system. In most of the cases (about 90%) they occur as a isolated tumour and only in 10% cases they occur in persons with neurofibromatosis type 1 (NF1),an autosomal dominant genetically inherited disease[1]. The thoracic cavity contains numerous nervous structures from which neurogenic structures may arise, but esophageal and intrapulmonary neurogenic tumour occur infrequently. Esophageal neurofibroma is a benign tumour accounts for only 0.9% all benign esophageal neoplasm[2]. On the other hand, pulmonary neurofibroma accounts for less than 1% of all lung neoplasm[3]. Therefore, concomitant presence of esophageal and pulmonary neurofibroma without neurofibromatosis type 1 is a extremely rare case to be presented. Herein, we described such a case confirmed by histopthologic examination and was managed surgically as per indication.

Case Report:

A 26 year old woman presented to the Thoracic Surgery department of National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka with painless, progressive dysphagia from solids to liquids, developed over a period of 4 months with sensation of sticking of food. She had no history of weight loss, appetite loss and symptoms of gastroesophageal reflux. She denied any history of corrosive ingestion, foreign

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body impaction, esophageal instrumentation or chest radiotherapy. She also had fever which occurred intermittently over the preceding 3 months; the fever was high grade, continued, not associated with evening rise of temperature or chill and rigor, subsides with paracetamol and used to recur 2-3 weeks later. She had no associated cough, dyspnea, productive sputum, haemoptysis or chest pain. She is a non smoker, non alcoholic and has no history of tobacco use or betel nut chewing. No family history of neurofibromatosis type-1. General examination and systemic examinations including alimentary system and respiratory system examination were unremarkable including absence of skin lesion that of neurofibromatosis type-1.

Routine laboratory investigations including complete blood count, liver and renal function tests were within normal range. Barium swallow X-ray of esophagus (fig-1) revealed narrowing in the midpart of esophagus with proximal dilatation with normal mucosal patterns. Upper gastroitestinal tract endoscopy disclosed narrowing of esophagus at 30 cm from upper incisor teeth with normal overlying mucosa and scope couldn't pass beyond the narrowing. CT scan of chest with contrast (fig-2) outlined a long segment circumferential wall thickening measuring about 17.6 mm in single wall thickness with luminal narrowing at mid and part of lower thoracic esophagus. Involved esophageal segment is approximately 82.2 mm in length and extending upto 16.4 mm proximal to gastro-esophageal junction. Proximal to this lesion esophagus was found dilated. There was sub segmental consolidation at posterior basal segment of lower lobe of right lung (fig-3). No associated mediastinal lymhadenopathy was present.Because of the refractory symptoms and long segment esophageal lesion, patient was

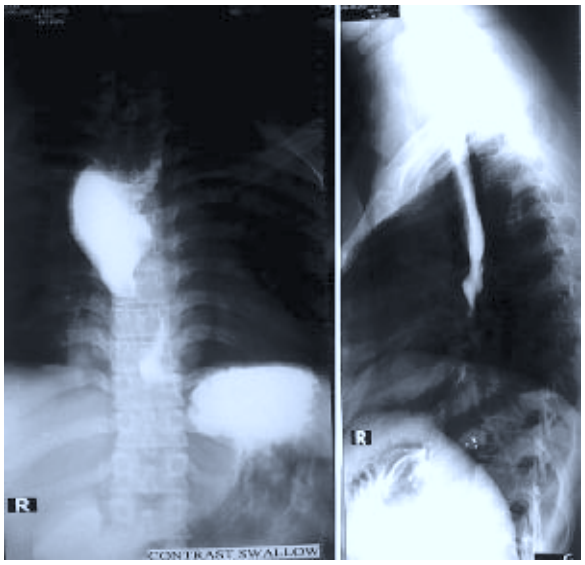

Fig-1: *Barium swallow X-ray of esophagus showing narrowing in the midpart of esophagus with proximal dilatation with normal mucosal patterns.*

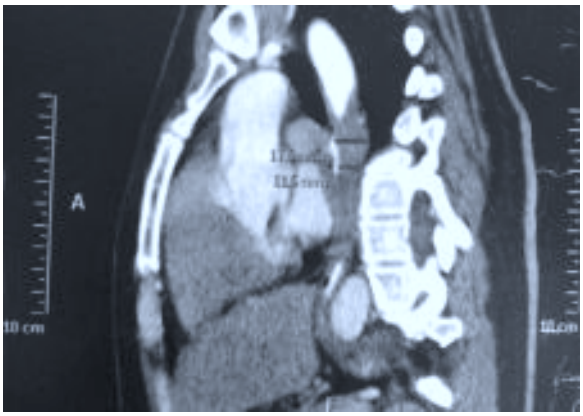

Fig-2: *CT scan of chest showing a long segment circumferential wall thickening with luminal narrowing at mid and part of lower thoracic esophagus.*

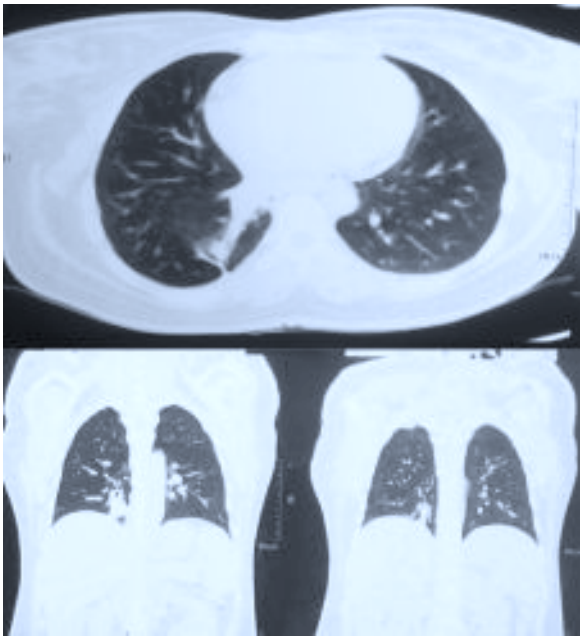

Fig-3: *Sub segmental consolidation at posterior basal segment of lower lobe of right lung*

prepared for two stage esophago-gastrectomy with esophago-gastrostomy. With all aseptic precaution under general anaesthesia abdomen was opened initially with upper midline incision and stomach was mobilized to use as esophageal substitute. Then in the next stage, standard right posterolateral thoracotomy done and chest cavity was accessed. A mass palapated within the lower lobe of right lung which was approximately 3cm x 2cm in size, firm in consistency, therefore right lower lobectomy was done. A mass was also palpated within the middle and part of lower 1/ 3rd of thoracic esophagus which was about 6cm x 2cm size, firm in consistency (fig-4). Esophago-gastrectomy was done containing the mass followed by intrathoracic esophago-

gastrostomy. There were no enlarged mediastinal lymph nodes detected. Both resected specimen, the esophagus and the lower lobe of right lung was sent for histopahology. The hispathology revealed that, macroscopically both the resected specimen of the esophagus and the lower lobe of right lung has a grey-white tumour within, microscopy showed it consists of spindle shaped cells with wavy nuclei, fibroblasts, collagen fibres, neuritis, blood vessels and absence of malignant cells; thereby esophageal neurofibroma and pulmonary neurofibroma was confirmed. The post operative period was uneventful. Post operative contrast swallow X-ray revealed no evidence of leakage from the anastomosis site and no evidence of esophageal narrowing. Post operative CT scan of chest was also satisfactory. Therefore, the patient was discharged on the 10th post operative day with advice including follow up schedule.

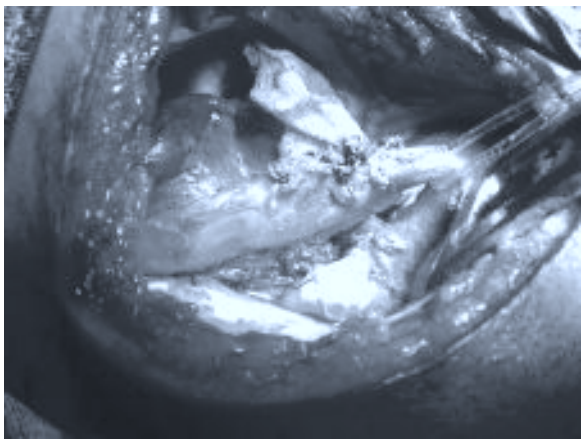

Fig-4: *A mass (Neurofibroma) in the middle and part of lower thoracic esophagus.*

Discussion:

Esophageal tumours are mostly malignant as benign tumors of the esophagus constitute less than 1% of esophageal neoplasms. Nearly two thirds of benign esophageal tumors are leiomyomas whereas neurofibroma are exceedingly rare[4]. Esophageal neurofibromas are of 3 types- localized, diffuse and plexiform. Localized and diffuse neurofibroma are associated with neurofibromatosis type 1 whreas localized neurofibroma usually occurs sporadically as in our patient and arise from Aurbach's plexus and Meissner's submucosal plexus in esophagus[5,6]. Esophageal neurofibroma may remain asymptomatic for years or may present with painless progressive dysphagia within a short period of months like our patient which is also supported by study of others[7,8]. Contrast esophagogram may be done initially to evaluate the patient with dysphagia. CT scan of chest with oral contrast helps to delinate the relationship between the tumour and surrounding structures and also detects mediastinal or extraesophageal pathology. Endoscopic assessment of esophagus is necessary to evaluate the degree of narrowing, condition of the mucosa and to take biopsy in suspicious lesion to rule out malignancy[9]. All the above mentioned tests were done in our case preoperatively except the endoscopy guided biopsy as the esophageal mucosa was healthy in our patient. Surgery is indicated in our patient as the tumour is more than 1cm and the patient is symptomatic[10,11]. Indication for surgery also includes increase in the size of the tumour during follow up. Our patient needed esophageal resection and esophago-gastric anastomosis for refractory symptomps which is also observed in the study of others[12]. Our patient also had pulmonary neurofibroma which may occur either as an endobronchial tumour where trachea being most common site followed by right sided lobar bronchi or may occur as a parenchymal mass like our case[7]. The sporadic pulmonary nerofibroma as in our patient is independent of neurofibromatosis type 1 and arise from bronchial submucosal nerves. A patient with pulmonary neurofibroma may remain asymptomatic similar to our case or may present with cough, dyspnea, wheezing, chest pain and even haemoptysis may occur due to hypervascular nature of the tumour. CT scan of chest, bronchoscopy and guided biopsy followed by

histopathology aid in establish the diagnosis.Depending upon the site and size of the tumour, pulmonary nerofibroma may require surgical resection including wedge resection, segmentectomy, lobectomy besides enucleation of the tumour and bronchoscopic resection[13]. Surgical resection of pulmonary neurofibroma is also indicated where diagnosis is uncertain preoperatively as in our case and also in cases where there is evidence of extrabronchial extension of the tumour or anticipated difficulty with bronchoscopic management including risk of haemorrhage because of hyper vascularity of the tumour[14]. Our patient needed lobectomy which is supported by other studies[13]. Histopathology confirms the diagnosis of pulmonary and esophageal neruofibroma in our patient that comprises spindle shaped cells with wavy nuclei associated with collagen fibrills which is also observed in study of others[2,8,13,15]. The patient had a uneventful intra operative and postoperative period with symptomatic improvement therefore discharged home accordingly.

Conclusion:

The concomitant occurrence of esophageal and pulmonary neurofibroma in our patient purely represent a rare coincidence as they are independent of neurofibromatosis type 1. However, it causes considerable problems preoperatively differentiating from malignant lesion because of their rarity as benign tumour in these organs. Therefore, histopathologic confirmation is done for proper management and follow up plan. Surgical resection usually cures the patients but patients still need to be evaluated during scheduled follow up for recurrence and malignant transformation although rare in sporadic neurofibroma as in this casse.

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INSTRUCTION TO AUTHORS ABOUT UNIFORM MANUSCRIPT WRITING

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