CLINICAL PROFILE AND OUTCOME OF SEVERE ACUTE RESPIRATORY ILLNESS (SARI) IN PATIENT WITH NON COVID 19 AETIOLOGY

Dr. Anupam Roy[1], Dr. Dipankar Das[2], Dr. Mrityunjay Roy[3], Dr. Syamal Kundu[4], Dr Manoranjan Ghosh*

[1]MBBS, MD (General Medicine), Bankura Sammilani Medical College, Bankura, West Bengal.
[2]Assistant Professor, Department of General Medicine, Bankura Sammilani Medical College, Bankura, West Bengal.
[3]Assistant Professor, Department of General Medicine, Bankura Sammilani Medical College, Bankura, West Bengal.
[4]Professor, HOD, Department of General Medicine, Bankura Sammilani Medical College, Bankura, West Bengal.
*MBBS, MS (General Surgery), MCh (Paediatric Surgery), Assistant Professor, Bankura Sammilani Medical College, Bankura, West Bengal.

Corresponding author: Dr Manoranjan Ghosh
MBBS, MS (General Surgery), MCh (Paediatric Surgery), Assistant Professor, Bankura Sammilani Medical College, Bankura, West Bengal.

Abstract

Introduction: Lower respiratory tract infections pose a substantial risk for humans due to high potential of dissemination in community. This disease cause high morbidity and mortality including higher rate of hospitalization as well as consumption of health care resources. Severe acute respiratory illness (SARI) is a common presenting features of many airborne respiratory pathogen. There has been recent surge of respiratory invasive viruses including Avian influenza, Middle East Respiratory Syndrome Corona virus (MERS-COV) and SERS COV 2 (Covid 19) in last decade leading to severe human illness and need for intensive care unit admissions .

Materials and methods: This is a observational, descriptive, longitudinal study will done in patients presenting with clinical feature of non-Covid SARI. After taking consent and through review of inclusion and exclusion criteria cases are enrolled in the study. All the participants will undergo evaluation through detailed history taking, clinical examination, laboratory investigations as per the defined research protocol and data generated there off are documented in case record sheets. Patients are followed till final outcome ie. Discharge or death.

Results: Maximum 54 (53.46%) cases are in the age group 38-58 years with Male : Female 2.53. Manual workers comprised 96% 0f total cases and smoking is noted in20.79% with in total cases. 61.38 % cases admitted in hospital after 7 days of onset of symptoms, where 38.61 % admitted within 7 days of symptoms onset. Maximum percentage (79.20%) of patients experienced intermittent type off ever with hectic temperature noted in 4.95 % 0f cases. Fever present at D1, D2, D3 82,47,5 respectively with in total number of cases (101). Percentage of patients (71.28%) had leukocytosis with 81.18% has thrombocytopenia during follow-up. Fifty patients (49.50 %) had elevated urea above upper normal limit. Fifty one patients had within normal limit. Serum creatinine raised in 46.53% of patients and normal in 52.47 %. CRP raised in 63.36% and rest are within normal limit. Patients with raised LDH level is 25.74% and 74.25 % are within normal range. Fifty five patients (54.45 %) had hyperferritinemia and 45.54% are within normal range. D dimer value raised in 74.26 % patients and normal in 25.74 % of cases.

Conclusion: Our study reveals negative correlation with inflammatory markers including Ferritin, LDH, D-dimer with outcome and no correlation with CRP. Very few studies addressed the issue of correlation of inflammatory markers with outcome in non Covid SARI. Our study in that respect is pioneering work in this region of country. There are several reports of positive correlation of inflammatory markers with poor outcome with SARI of non Covid aetiology. In our study SARI presentation is caused by several different aetiologies including bacterial pneumonia, dengue pneumonia, scrub pneumonia, tubercular pleural effusion, SOL and pneumonia of undefined which is maximum.

Key Words: Lower respiratory tract infections, Severe acute respiratory illness, Ferritin, LDH, D-dimer.

INTRODUCTION

Lower respiratory tract infections pose a substantial risk for humans due to high potential of dissemination in community. This disease cause high morbidity and mortality including higher rate of hospitalisation as well as consumption of health care resources.[1] Severe acute respiratory illness (SARI) is a common presenting features of many airborne respiratory pathogen. There has been recent surge of respiratory invasive viruses including Avian influenza, Middle East Respiratory Syndrome Corona virus (MERS-COV) and SERS COV 2 (Covid 19) in last decade leading to severe human illness and need for intensive care unit admissions.[2]

Clinical presentations of SARI has been recognized as presenting features in many other non viral pathogens eg:- community acquired pneumonia ,atypical bacterial pneumonia and fungal pneumonia. During the covid pandemic time SARI was noted as the most common presentation for hospital admission. In the later phase of covid pandemic there was resurgence of bacterial pneumonia and fungal pneumonia including mucormycosis and invasive pulmonary aspergillosis. Atypical pneumonia especially scrub typhus occur in few regional pockets in india throughout the year. Hence SARI is a common clinical features of multitude of organism other than covid infections during covid pandemic.
Clinical profile of SARI has been less studied in this region of the country. Relative incidence of different respiratory pathogens vary in geographical region of India due to biodiversity as well as variation in populations characteristics .There has been no study on clinical profile of non Covid SARI in south west part of West Bengal, India. Clinical documentation of this particular entity may lead to better understanding as well as risk stratification vis-a-vis effective management.

AIMS & OBJECTIVES

AIM:

To document clinical profile and outcome of severe acute respiratory illness (SARI) in patient with non covid 19 aetiology.

Objective:

General objectives:

To describe epidemiological profile, clinical presentation and outcome of patients with non covid SARI.

Specific objectives:

a) To describe demographic profile, clinical presentation and course of study population.

b) To document aetiology of SARI as per available resources of the hospital.

c) To document outcome of above patients in terms of hospital stay, organ dysfunction, residual organ dysfunction at discharge and death on standard treatment as per aetiology.
d) To workout correlation of inflammatory markers with outcome (serum Ferritin, LDH, CRP, D-Dimer).

MATERIALS AND METHODS

Type of study –This is a observational, descriptive, longitudinal study.

Place of study –In patient department of General Medicine, Bankura Sammilani Medical College and Hospital.
Period of study–18 months.

Study population–All adult patients admitted with diagnosis of non Covid SARI in General Medicine Ward during study population.
Sample size/design –targeted 103 patients.

The sample size will be calculated using following formula for cross sectional study:

$$\text{It is } n=Z2 \times P\times Q/L2$$

Where Z=1.96 at 95% confidance interval.

P= Prevalence of event of interest (non covid SARI)≅61 %(22)

Q= Complement of P= (100-P)

L=Accepted error, here it is assume to be 10 (absolute)

(1.96)2x61x39/100 ≅92

Considering 10% refusal, the final sample size will be (92*100/90)≅103

Data collection of proposed study will be done for 1 year, that is 52 weeks. Data collection will be done twice a week and data collection will be chosen at the beginning of week via simple random sampling using lottery method.
Case, control required or not-not required.

Inclusion criteria: All adult patient (>17 years) with confirming clinical criteria of SARI and covid RTPCR negative admitted in BSMCH during the study period.

Exclusion criteria: Comorbidities e.g. Diabetes, HTN, chronic visceral dysfunction, Chronic respiratory disease and malignancy. Patients not willing to participate in this study.

Study design: This is a observational, descriptive, longitudinal study will done in patients presenting with clinical feature of non-Covid SARI. After taking consent and through review of inclusion and exclusion criteria cases are enrolled in the study. All the participants will undergo evaluation through detailed history taking, clinical examination, laboratory investigations as per the defined research protocol and data generated there off are documented in case record sheets. Patients are followed till final outcome ie. Discharge or death. The collected deta are finally compiled in a master chart and presented for statistical

analysis as per the grant chart given below.
Study of clinical sample and keeping original records of individual patients. Record keeping and compliance of data. Computation of statistical figures, making of chart and graphs. Final work and construction of the study.

Laboratory investigation, parameters and procedure: Hematological and biochemical examination of blood. Blood for CBC, LFT, sugar (FBS, PPBS) Urea and Creatinine. ESR, CRP, Neutrophil lymphocyte ratio, Blood culture, ABG, chest x ray, HRCT thorax, USGW/A, CRP Ferritin, LDH D-dimer level at day 1,3,6. Sputum for True Nat for detection of Tuberculosis.

RESULTS

TABLE 1: DISTRIBUTION OF STUDY PATIENTS AS PER AGE

AGE GROUP (In years)	FREQUENCY	PERCENTAGE
17-37	26	25.74%
38-58	54	53.46%
59-78	21	20.79%
TOTAL	101	100%

CHART 1: DISTRIBUTION OF STUDY PATIENTSAS PER AGE

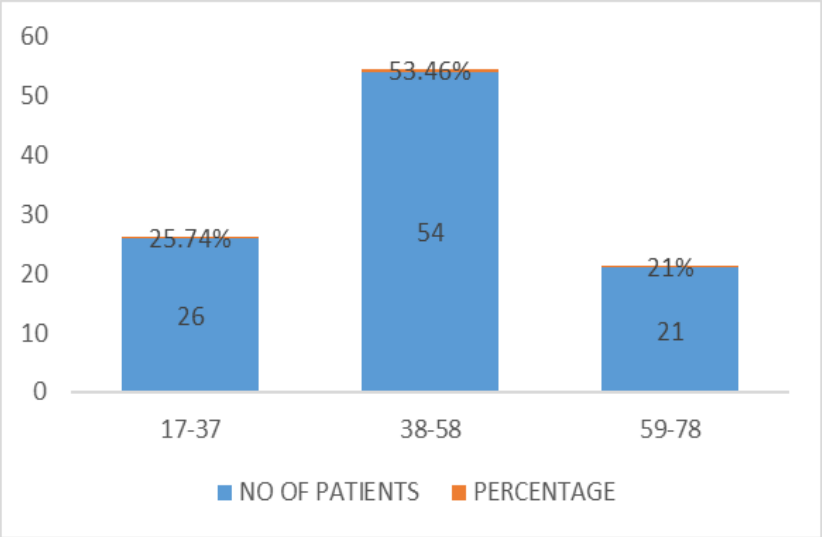

TABLE 2: DISTRIBUTION OF STUDY PATIENTS AS PER SEX

SEX	FREQUENCY	PERCENTAGE
MALE	72	71.28%
FEMALE	29	28.71%
TOTAL	101	100 %

CHART 2: DISTRIBUTIONOFSTUDY PATIENTSAS PER SEX

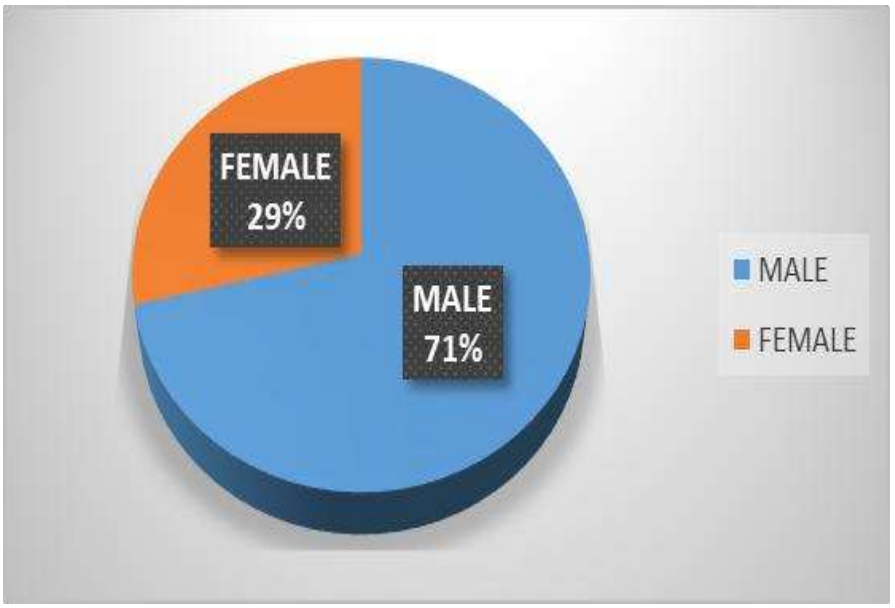

TABLE 3: OCCUPATION WISE DISTRIBUTION OF STUDY POPULATION

OCCUPATION	FREQUENCY	PERCENTAGE
MANUAL	97	96.03%
INTELLECTUAL	4	3.96%
TOTAL	101	100%

CHART 3: OCCUPATION WISE DISTRIBUTION OF STUDY PATIENT

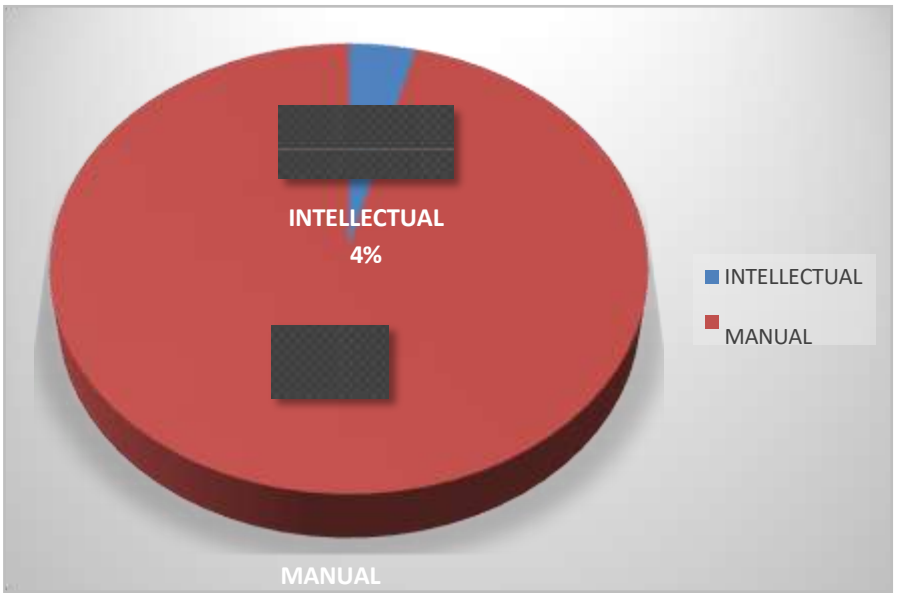

TABLE 4: DISTRIBUTION OF STUDY PATIENT AS PER SMOKING HABIT

SMOKING HABIT	FREQUENCY	PERCENTAGE
YES	21	20.79%
NO	80	79.21%
TOTAL	101	100%

Maximum 54 (53.46%) cases are in the age group 38-58 years with Male: Female 2.53. Manual workers comprised 96% 0f total cases and smoking is noted in 20.79% with in total cases.

CLINICALPROFILE

TABLE 5: DISTRIBUTION OF PATIENT AS PER SYMPTOM ONSET TO ADMISSION TIME PERIOD

SYMPTOM ON SET TO TIME OF ADMISSION	FREQUENCY	PERCENTAGE
<7 DAYS	39	38.61%
>7 DAYS	62	61.38%
TOTAL	101	100%

TABLE 6: DISTRIBUTION OF PATIENT AS PERFEVER PATTERN

FEVER PATTERN	FREQUENCY	PERCENTAGE
INTERMITTENT	81	80%
REMITTENT	15	15%
HECTIC	5	4.95%
TOTAL	101	100%

TABLE 7: DISTRIBUTION OF STUDY PATIENT AS PER FEVER PROFILE AT DAY 1, 3, 6

FEVER	DAY1	DAY3	DAY6
PRESENT	82	47	5
ABSENT	19	54	96

Above table and bar diagram reveals that 61.38 % cases admitted in hospital after 7 days of onset of symptoms, where 38.61 % admitted within 7days of symptoms onset. Maximum percentage (79.20%) of patients experienced intermittent type off ever with hectic temperature noted in 4.95 % 0f cases. Fever present at D1, D2, D3 82,47,5 respectively with in total number of cases (101).

LABORATORY PARAMETERS

TABLE 8: DISTRIBUTION OF PATIENT AS PER WBC COUNT AT ADMISSION

WBCCOUNT (10^9/L)	FREQUENCY	PERCENTAGE
<4000	29	28.71%

>11000	72	71.28%
TOTAL	101	100%

TABLE 9: DISTRIBUTION OF STUDY PATIENT AS PER PLATELET COUNT

PLATELET COUNT(10^3/microlit)	**FREQUENCY**	**PERCENTAGE**
<150000	19	18.81%
150000-400000	82	81.18%
TOTAL	101	100%

TABLE 10: DISTRIBUTION OF PATIENT AS PER SERUM UREA LEVEL

UREA (mg/dl)	FREQUENCY	PERCENTAGE
>30	50	49.50%
<30	51	50.49%
TOTAL	101	100%

TABLE 11: DISTRIBUTION OF PATIENT AS PER SERUM CREATININE

CREATININE (mg/dl)	FREQUENCY	PERCENTAGE
>1.2	47	46.53%
<1.2	54	53.46%
TOTAL	101	100%

TABLE 12: DISTRIBUTION OF STUDY PATIENT AS PER SGOT

SGOT(unit/L)	**FREQUENCY**	**PERCENTAGE**
>40	43	42.57%
<40	58	57.42%
TOTAL	101	100%

TABLE 13: DISTRIBUTION OF STUDY PATIENT AS PER SGPT

SGPT(u/L)	FREQUENCY	PERCENTAGE
>56	30	29.70%
<56	71	70.29%
TOTAL	101	100%

TABLE 14: DISTRIBUTION OF PATIENT AS PER CRP

CRP(mg/L)	FREQUENCY	PERCENTAGE
≥10	64	63.36%
<10	37	36.63%
TOTAL	101	100%

TABLE 15: DISTRIBUTION OF PATIENT AS PER FERRITIN VALUE

FERRITIN(□g/L)	FREQUENCY	PERCENTAGE
>330	55	54.45%
<330	46	45.54%
TOTAL	101	100 %

TABLE 16: DISTRIBUTION OF PATIENT AS PER LDH VALUE

LDH (Unit/L)	FREQUENCY	PERCENTAGE
≥333	26	25.74%
<333	75	74.25%
TOTAL	101	100%

TABLE 17: DISTRIBUTION OF STUDY PATIENT AS PER D DIMER VALUE

D DIMER (□/ml)	FREQUENCY	PERCENTAGE
<0.5	26	25.74%
≥0.5	75	74.26%
TOTAL	101	100%

Percentage of patients (71.28%) had leukocytosis with 81.18% has thrombocytopenia during follow-up. Fifty patients (49.50 %) had elevated urea above upper normal limit. Fifty one patients had within normal limit. Serum creatinine raised in 46.53% of patients and normal in 52.47 %. CRP raised in 63.36% and rest are within normal limit. Patients with raised LDH level is 25.74% and 74.25 % are within normal range.

Fifty five patients (54.45 %) had hyperferritinemia and 45.54% are within normal range. D dimer value raised in 74.26 % patients and normal in 25.74 % of cases.

ETIOLOGY

TABLE 18: DISTRIBUTION OF PATIENT AS PER RADIOLOGICAL FEATURE (HRCT THORAX)

	RADIOLOGICAL FEATURE	Frequency	Percentage
	Alveolar Pneumonia	54	53.5
	Interstitial pneumonia	20	19.8
	Mixed pattern pneumonia	8	7.9
	No abnormality	4	4.0
	Pleural effusion	9	8.9
	SOL	6	5.9
	Total	101	100.0

TABLE 19: PATHOLOGICAL DISTRIBUTION OF STUDY PATIENT

PATHOLOGY	FREQUENCY	PERCENTAGE
PNEUMONIA	82	81.18%

PLEURAL EFFUSION	9	8.91%
SARI with SOL	6	5.94%
SARI with normal HRCT	4	3.96%
TOTAL	101	100%

TABLE 20: AETIOLOGY WISE DISTRIBUTION OF STUDY PATIENT

AETIOLOGY	FREQUENCY	PERCENTAGE
BACTERIAL PNEUMONIA	28	27.72%
SCRUB PNEUMONIA	9	8.91%
DENGUE PNEUMONIA	6	5.94%
PNEUMONIA of UNDEFINED AETIOLOGY	39	38.61%
TUBERCULAR PLEURAL EFFUSION	5	4.95%
UNDEFINEDPLEURALEFFUSION	4	3.96%
SARI with SOL	6	5.94%
SARI with normal HRCT	4	3.96%
TOTAL	101	100%

Twenty eight patients (27.72%) of study patient has bacterial pneumonia, 9 (8.91%) scrub pneumonia and maximum number 39 (38.61%) with pneumonia of undefined etiology. In radiological features HRCT thorax scan shows 53.5% of patients had alveolar pneumonia, 19.8% patients had interstitial pneumonia, 7.9% patients had mixed pattern pneumonia and 8.9% patients had pleural effusion. We also found 3.96% with normal HRCT scan.

CORRELATION OF INFLAMMATORY MARKERS WITH OUTCOME

TABLE 26: CORRELATION OF CRP WITH OUTCOME

OUTCOME GROUPS	FREQUENCY	MEAN	STANDARD DEVIATION (SD)	CORRELATION COEFFICIENT	p-value
<10Days	83	37.12	33.72395	0.014	0.891
≥10Days+Death	18	38.42	34.11768		

Pvalue0.891 -**Statistically not significant**

TABLE 27: CORRELATION OF SERUM FERRITIN WITH OUTCOME

OUTCOME GROUPS	FREQUENCY	MEAN	SD	CORRELATION COEFFICIENT	p-value
<10Days	83	382.84	222.461	-0.129	0.200
≥10Days+Death	18	304.93	170.017		

Pvalue0.200 -**Statistically not significant**

Table 28: CORRELATION OF LDH WITH OUTCOME

OUTCOME GROUPS	FREQUENCY	MEAN	SD	CORRELATION COEFFICIENT	p-value
<10Days	83	270.28	136.031	-0.068	0.515
≥10Days+Death	18	246.47	85.272		

P value 0.515 -**Statistically not significant.**

Table 29: CORRELATION OF D DIMER WITH OUTCOME

OUTCOME GROUPS	FREQUENCY	MEAN	SD	CORRELATION COEFFICIENT	p-value
<10Days	83	1.5533	1.79405	-0.136	0.177
≥10Days+Death	18	0.9153	0.60138		

P value 0.177- **Statistically not significant.**

There is no statistical significant relation between inflammatory markers (CRP, Ferritin, LDH, D-dimer), as the P value of CRP, Ferritin, LDH, D-dimer values are 0.891, 0.200, 0.515 and 0.177

respectively (P value <0.05- statistically significant). Although there is no statistical relationship, negative correlation between inflammatory markers and outcome was found.

DISCUSSION

In our study 53.46% patients (maximum) belongs to age group 38 to 58 years and 20.79 % (minimum) in above 58 years with a M:F 2.53. Kristen Fagerli, Mukhchulunnuljiibayar etal. conducted a study on epidemiology of pneumonia in hospitalized adults ≥ old showed almost similar results. They report maximum percentage of pneumonia admission in age group between 26-45 years with M: F 0.9.This study quite similar with our of study with age specific incidence of pneumonia but also opposes as with more percentage is associated with female population. Gender differences in occupation, tobacco and alcohol use, and other environmental exposures likely contribute to predominance of pneumonia in men. Men generally participate in more outdoor manual labor than women, increasing their exposure to occupational air pollutants and ambient air pollution. Christian Theilacker, Ralf Sprenger, et al. conducted a study on Population-based incidence and mortality of community-acquired pneumonia, in Germany reveals 33.5% study population were 60 years or older which is slightly differs from our study as our study comprised of 20.79% of population with age group above 58 years. This difference observed may be because of there is different in inclusion and exclusion criteria.

As per the occupation and smoking habit 97(96%) patients was manual worker and Patients (4%) intellectual worker with a smoker 20.79% and non smoker 79.21%. (Hyejung Jung, Dong-HeeKoh, SangjunChoi, Ju-Hyun Park, Hwan-Cheol Kim, Sang-Gil Lee, and Donguk Parket al. conducted a study where they found 32.47 % labor force associated with smoking. Intellectual workers are lowest affected by SARI because there may be difference in occupation and work environment. There may be less percentage of non smoker because of demographic variation in different geographical region.

Clinical profile

Patient admitted after 7 days of symptom onset are 62 (61.38%). Patients with intermittent fever is maximum percentage (80%) and hectic temperature noted in 4.95 % cases are observed. As per fever profile fever present on D2 is 47 (46.53%), D3 is 5 (4.95%) which is significantly less than 82(81.18%) patients on-D1ofhospital admission. As most of the cases of lower respiratory tract infection becomes symptoms free within 7 days, incidence of hospital admission in maximum number of patients in our study indicates lack of education and poor socio-economic status in our region.

Laboratory parameters.

Patients with leucocytosis are 72(71.28%) and 19 (18.81%) are associated with thrombocytopenia. (Raymond S M Wong, Alan Wu, ,K F To, Nelson Lee, Christopher W K Lam, et al. conducted a study on Haematological manifestations in patients with severe acute respiratory syndrome: retrospective analysis is similar to our study[56]). They reported neutrophilia in (82%), thrombocytopenia in patients (55%) in theie study. Dong-Min Kim, Seok Won Kim,Seong-Hyung Choi, and Na Ra Yun; conducted

a study on Clinical and laboratory findings associated with severe scrub typhus and they reported leucocytosis their study69.Thereare 36.6 % of patient developed acute kidney injury in respect to BUN and creatinine ratio. (Masao Iwagami, Kathryn Mansfield, Jennifer Quint, Dorothea Nitsch, and Laurie Tomlinson as per our study). Patients with raised inflammatory markers as per CRP, Ferritin, LDH, D-Dimer are 64(63.36%), 55(54.45%), 26(25.74%), 75(74.26%) respectively. Maximum number is associated with D dimer and minimum is LDH. Sulhattin Arslan, Serdal Ugurlu, Gokten Bulut, Ibrahim Akku; conducted a clinical study on association between Plasma D-dimer Levels and Community-Acquired Pneumonia; they reported that CAP patients show increased plasma DD levels even in the absence of an accompanying disease that can increase D- dimer levels.

Aetiology

As per radiological features maximum number of patient (53.5%) of alveolar pneumonia and 4% with no abnormalities. We found several aetiology of SARI in our study population. Maximum number of patient with pneumonia of undifferentiated aetiology (38.61%), bacterial pneumonia (27.72%), scrub pneumonia (8.91%) , dengue (5.94%) and pleural effusion of (8.91%),in which 4.95% are tubercular and 3.98% are undefined and also SOL(5.9%).

Outcomes and its correlation with inflammatory markers

In our study, we divided the study population in two groups (good outcome- hospital stay<10 days and poor outcome–hospital stay >10 days + death). During the covid pandemic there are several study with inflammatory markers with outcome in covid 19 pneumonia but there is very few studies about correlation of inflammatory markers with outcome in non Covid SARI. In our study we did not find any statistically significant relation of inflammatory markers (CRP, Ferritin, LDH, D dimer) with outcome groups but they are negatively correlated except CRP which has minimal positive correlation. After statistical analysis we found maximum number 83 (82.17%) of patients those who are associated with hospital stay <10 days correlated negatively with inflammatory markers indicate that increase value of this markers associated with hospital stay >10 days in terms of poor outcome. Other outcome group (17.82%) shows hospital stays 10 days + death associate without increasing of inflammatory markers (Ferritin, LDH, D-Dimer). This difference in correlation within less percentage (17.82%) of cases documented may be due to others factors responsible for longer hospital stay and mortality eg. Sepsis, ARDS, multi organ dysfunction. Raymond Farah, Rola Khamisy-Farah, NicolaMakhoul Fernando Saldías-Peñafiel**,** Gerardo Salinas-Rossel**,** KatiaFarcas-Oksenberg et al. RuohanDanSu**,** Jiamei Li**,** Jiajia Ren**,** Ya Gao Li; conducted similar study as per our study.

CONCLUSION

Our study reveals negative correlation with inflammatory markers including Ferritin, LDH, D-dimer with outcome and no correlation with CRP. Very few studies addressed the issue of correlation of inflammatory markers with outcome in non Covid SARI. Our study in that respect is pioneering work in this region of country. There are several reports of positive correlation of inflammatory markers with poor outcome with SARI of non Covid aetiology. In our study SARI presentation is caused by several

different aetiologies including bacterial pneumonia, dengue pneumonia, scrub pneumonia, tubercular pleural effusion, SOL and pneumonia of undefined which is maximum. SARI with normal HRCT also present. Although the statistical results of this mixture group come to be not significant, correlate with outcome in terms of hospital stay and death Sub group analysis could have been better way of revealing correlation of inflammatory markers in different aetiology.

LIMITATION OF THE STUDY

Our study is a preliminary and first of this kind study in West Bengal. This is a single -hospital based study with small number of study population which may not be the true representative of SARI cases in this region. A further multicentric study across the state with larger study population is necessary to substantiate the validity of our study.

REFERENCES

1. VosT, LimSS, Abbafati C et al. Global burden of 369 diseases and injuries in 204 countries andterritories,1990â€-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020; 396: 1204-1222.
2. GBD 2013 Mortality and Causes of Death Collaborators Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990â€—2013: a systematic analysis for the Global Burden of Disease Study 2013.Lancet. 2015; 385: 117-171
3. CDC et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. MMWR Recomm Rep 2010;59(No. RR- 8):1â€-62. PubMed
4. Avian influenza viruses (AIV) are an ongoing risk to domestic pet,exotic(zoo)and wild birds worldwide. Encyclopedia of virology(Fourth Edition,2021)
5. Crofton and Douglas's Respiratory Diseases, Fifth Edition
6. Ali M. Zaki, M.D., Ph.D., Sander van Boheemen, M.Sc., Theo M. Bestebroer, B.Sc., Albert D.M.E. Osterhaus, D.V.M.,Ph.D.,and RonA.M.Fouchier, Ph.D. et al. Isolation of a Novel Corona virus from a Man with Pneumonia in Saudi Arabia, N Engl J Med 2012; 367:1814-1820
7. Goldsmith, CS, Tatti KM, Ksiazek TG, Rollin PE, Comer JA, Lee WW, et al. Ultrastructural characterization of SARS coronavirus. Emerg Infect Dis [serial online] 2004 Feb.
8. Abraham S., Kienzle T.E., Lapps W., Brian D.A. Deduced sequence of the bovine corona virus spike protein and identification of the internal proteolytic cleavage site. Virology. 1990;176:296â€—301.
9. M K Sen 1 , U C Ojha, S Chakrabarti, J C Suri :Dengue hemorrhagic fever (DHF) presenting with ARDS 1999 Apr-Jun;41(2):115-9.
10. L.C.S. Lum, M.K. Thong, Y.K. Cheah& S.K Lam:Dengue-associated adult respiratory distress syndrome,13 Jul 2016.