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Trends of variation of the laboratory parameters during the course of COVID-19 Illness

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ABSTRACT

Background: The coronavirus pandemic which had its origin in the Wuhan China has been spreading across the globe with far reaching complications and a variable clinical course. A variation of the laboratory parameters during the disease course remains a constant parameter to monitor the disease course and progression. Since the laboratory parameters are standardized globally, these may also act as uniform guidelines for the patients monitoring and treatment. **Aims and Objectives:** The aim of the study was to serial charting of the laboratory parameters in the recovered and expired patients of COVID-19 and to determine an associated prognostic significance. **Materials and Methods:** A retrospective observational study from the laboratory and medical records was conducted on the patients admitted from March 17, 2020, to May 31, 2020, at the tertiary care center dedicated to the treatment of RT-PCR confirmed COVID-19 positive patients. **Results:** The group of parameters showing a poor prognosis include a rising WBC count, high neutrophilic percentage, low lymphocyte percentage ($<$10) an NLR $>$ 15, low lymphocyte monocyte ratio $<$ 3, rising blood urea nitrogen, serum creatinine levels, and serum electrolyte levels. The liver function tests variation reflecting a poor metabolic activity of the liver, namely, a low serum albumin and albumin globulin ratio, rising SGOT levels, and total bilirubin levels. A highly significant variation in the acute phase reactants showing an exponential rise such as the serum lactate dehydrogenase levels, serum ferritin, fibrinogen, C-reactive protein, and IL 6 levels an increased level of D Dimer ($>$3) and a prolongation of the APTT. **Conclusion:** The variation of the laboratory parameters acts as a fair marker for the disease progression. Since the disease shows a variable progression with a sudden worsening of the clinical symptoms, a comprehensive monitoring of the laboratory parameters serves to diagnose and treat the disease progression.

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Key words: COVID-19; Laboratory parameters; Comparison

INTRODUCTION

The coronavirus pandemic has been spreading across the globe with far reaching complications and a variable clinical course. While the virus presents with varying clinical presentation with each wave, the variation of the laboratory parameters during the disease course helps to monitor the disease course and progression.

Aims and Objectives

1) To study the variation of the laboratory parameters from the hospital records of the patients admitted to a tertiary care hospital dedicated to the treatment of the patients with a Corona Virus infection as confirmed by a positive RT PCR test.
2) To analyze the variation of the laboratory parameters amongst the recovered & the expired patients.

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MATERIALS AND METHODS

A retrospective observational study from the laboratory and medical records was conducted on the patients admitted from March 17, 2020, to May 31, 2020, during the first wave of the disease, at the tertiary care center dedicated to the treatment of RT-PCR confirmed COVID-19 positive patients, after obtaining the institutional review board approval on June 10, 2020. Out of a total of 2739 patients admitted, consecutive 241 expired and 530 recovered patients were shortlisted of which 39 expired and 47 recovered patient's data were analyzed, after applying the inclusion and the exclusion criteria and their data. The statistical analysis was done using software SPSS 20.0 from IBM.

Machines and reagents

The routine blood tests and the biochemistry parameters and the acute phase reactants were carried out on the Siemens ADVIA – 2120, SIEMENS ADVIA 1800, Mindray BS- 200 and SIEMENS ADVIA Centaur XPT automated biochemistry analyzer, respectively.

RESULTS

The mean age of the patients was 62.62 (±14.42) and 37.83(±14.71) years, with a M: F ratio of 4:1 and 2:1 in the expired and the recovered patients, respectively, (Table 1, Figure 1a and b).

A progressive rise in the total WBC count and the neutrophil percentage, a decline in lymphocyte percentage and a lower monocytes percentage, along with a low lymphocyte monocyte ratio (LMR <3) and high neutrophil lymphocyte ratio (NLR >3) in the expired patients (Figure 2a). An insignificant variation in the levels of hemoglobin, platelets, RDW, and hematocrit levels was seen (Figure 2b).

High blood urea nitrogen (BUN), serum creatinine levels, and serum electrolytes were seen in the expired patients with a significant variation (Figure 3).

Serum albumin globulin ratio, serum albumin levels, total serum protein, alkaline phosphatase, serum aspartate transaminase (AST), and the total bilirubin were high with a significant variation (Figure 4a and b) while direct bilirubin,

Table 1: Variation of parameters during the disease and its significance

Parameters	Early	Middle	Late	P-value
Total WBC			>15000	<0.00001
Neutrophil %			>85	<0.00001
Monocytes%			<5	0.006
Lymphocytes %			<10	<0.00001
LMR			<2	<0.00001
NLR			>15	<0.00001
RDW			>15	0.73
Hct				0.20
Hb				0.055
Platelets				0.98
BUN			> 110	<0.00001
Se Creatinine			> 2	<0.00001
Se Sodium	Constant			0.007
Se Potassium	Constant			<0.00001
Se Chloride				0.96
Total Bilirubin				0.002
SGPT/ALT	>80			0.10
SGOT/AST	>110			0.043
Se Protein			<5.7	0.005
Alb:Glo ratio			<1.5	<0.00001
Se Globulin				0.204
Indirect Bilirubin				0.209
Direct Bilirubin			>0.3	0.376
Se Alk Phosphatase			>145	0.002
Se Albumin			<3.1	0.0001
IL6	>500			0.33
Se Ferritin		>950 (>3×)		<0.00001
LDH			>600 (>3×)	0.0001
CRP			>55 (>90×)	0.027
Troponin C	>20 times			0.085
D Dimer	>3			0.019
APTT		>50		< 0.00001
Fibrinogen			>900 (>2×)	< 0.00001

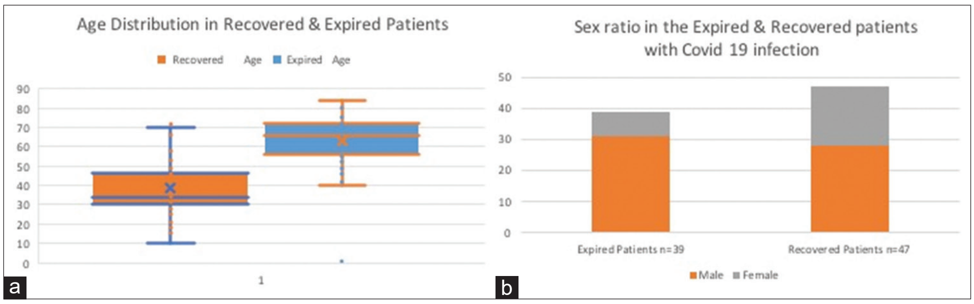

Figure 1: (a) The expired patients had a higher age distribution (median 66 years) compared Recovered patients (median 34 years). (b) The expired patients had a higher M:F sex ratio being 3.87:1 compared to 1.47:1 in the recovered patients

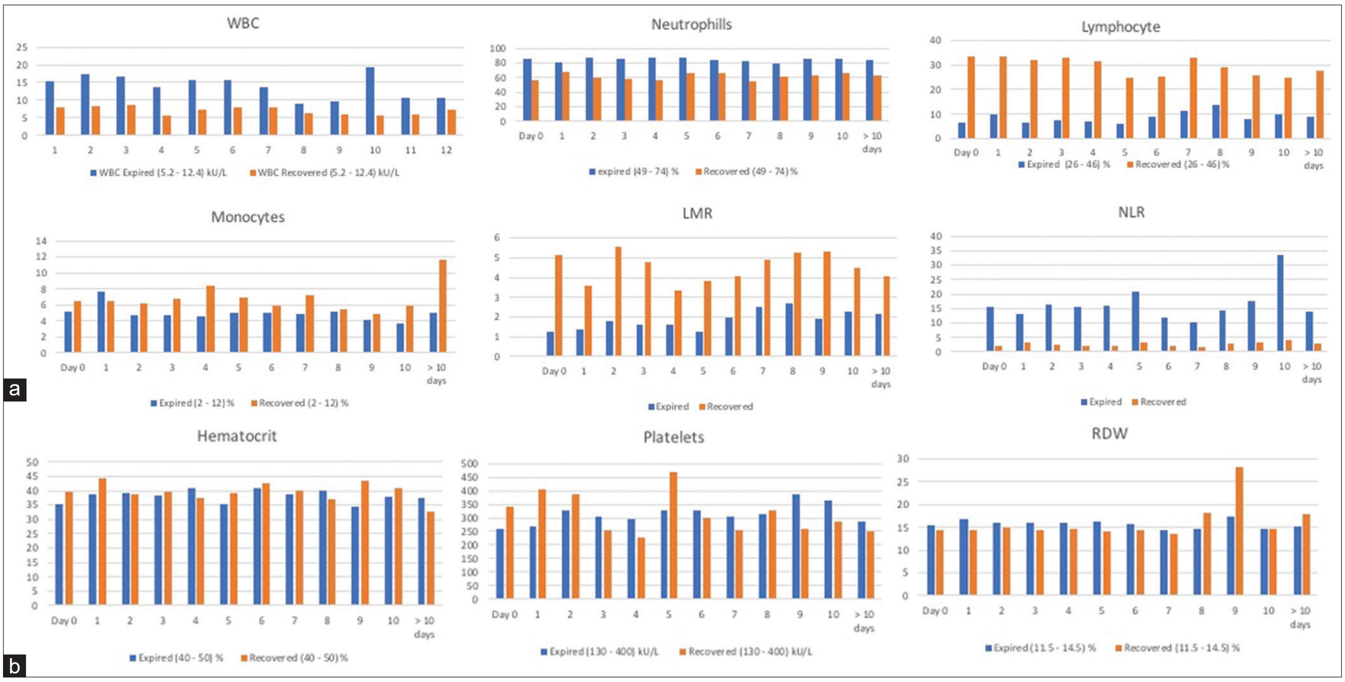

Figure 2: (a) A statistically significant variation was seen in the levels of total WBC, high neutrophil, low lymphocyte and lower monocytes levels with a significant variation in the LMR (<3) and the NLR ratio and a lower Hemoglobin levels in the expired patients. (b) The hematocrit levels, platelet levels and the RDW show a statistically non-significant variation, although a low hematocrit and higher RDW was seen in the expired patient

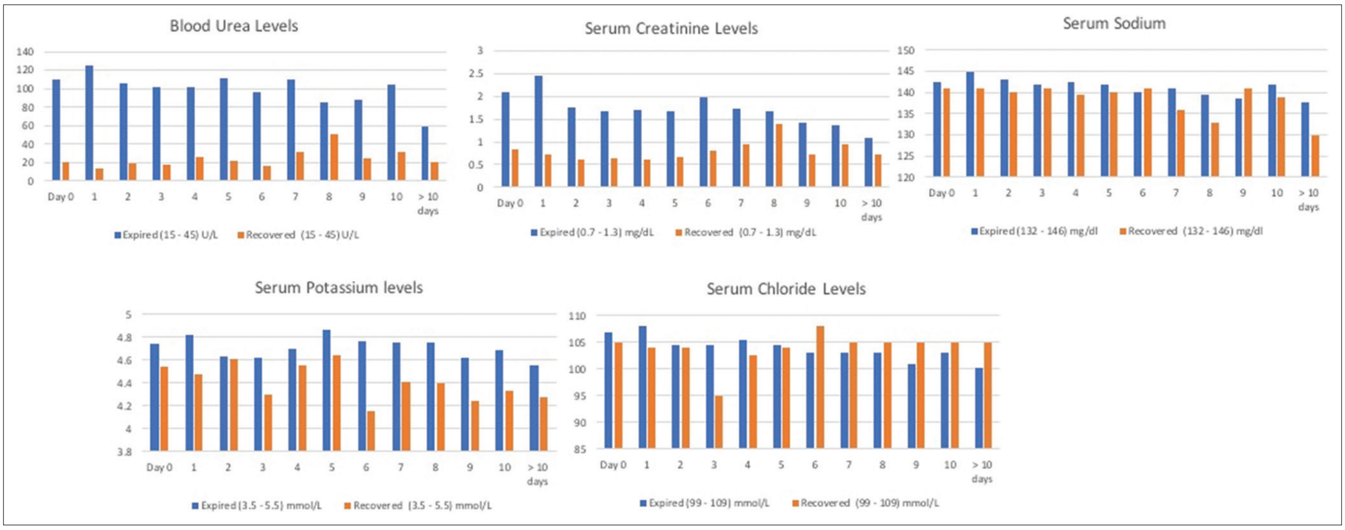

Figure 3: Renal function tests. The blood urea and serum creatinine levels and the serum electrolytes showed a statistically significant variation, with an increased level in the expired patients increasing more towards the terminal disease phase

serum globulins, and serum alanine transaminase showed an insignificant variation.(Figure 4c).

Serum ferritin, lactate dehydrogenase (LDH), C-reactive protein (CRP), and serum fibrinogen levels showed a highly significant variation (Figure 5).

A highly significant variation was seen in the D dimer and APTT levels (Figure 6).

DISCUSSION

The worldwide trend of age distribution pattern in COVID-19 positive patients ranges from a mean of 40–60 years.[1-3]

An increased WBC count and neutrophils percentage along with a reduced lymphocyte and platelets counts in severe and fatal COVID-19 disease.[2,4,5] A few studies reported a low WBC count in the disease.[6-8]

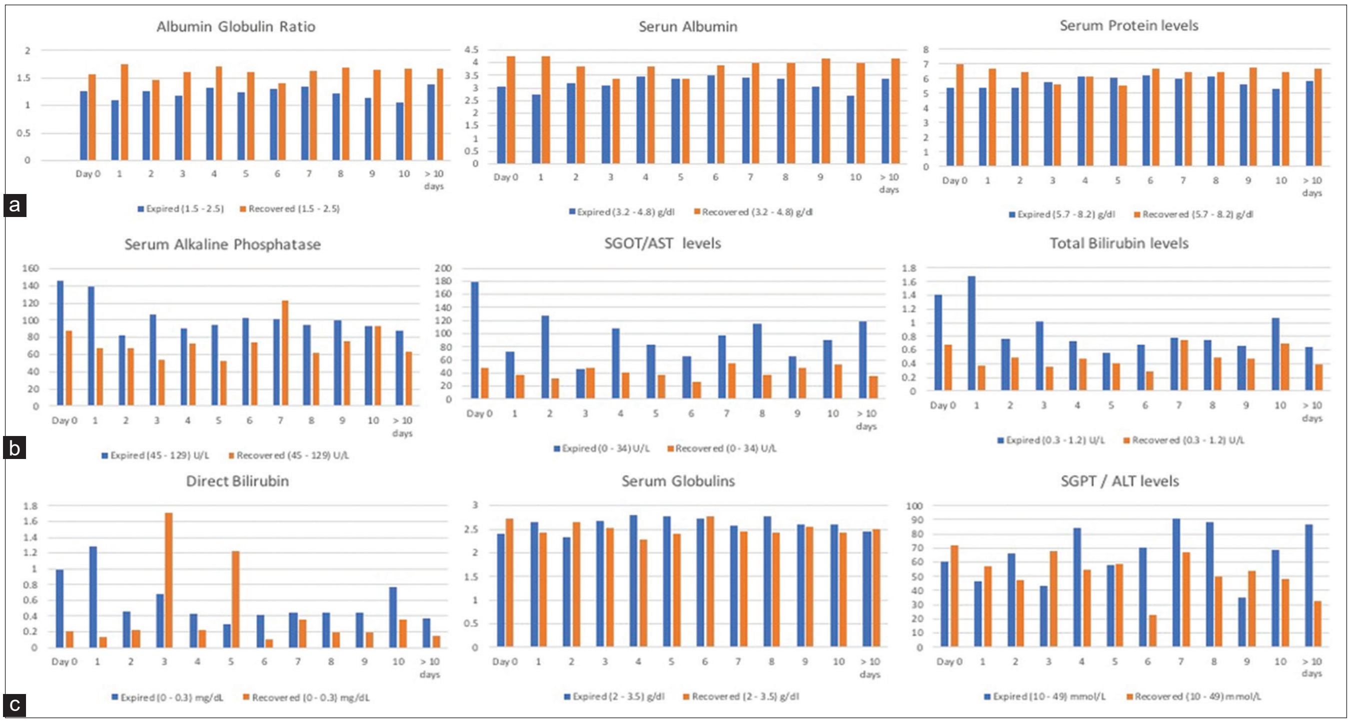

Figure 4: (a) A highly significant statistical variation was seen in the albumin globulin ratio, serum albumin levels and total protein levels, particularly in the imminent terminal disease phase in the expired patients. (b) The liver enzymes including the alkaline phosphatase and sgot along with the total bilirubin levels showed a significant statistical variation, with a consistently higher levels of the enzymes in the imminent terminal disease phase in the expired patients. (c) No significant statistical variation in the levels of Direct Bilirubin, Serum globulins and SGPT levels was seen

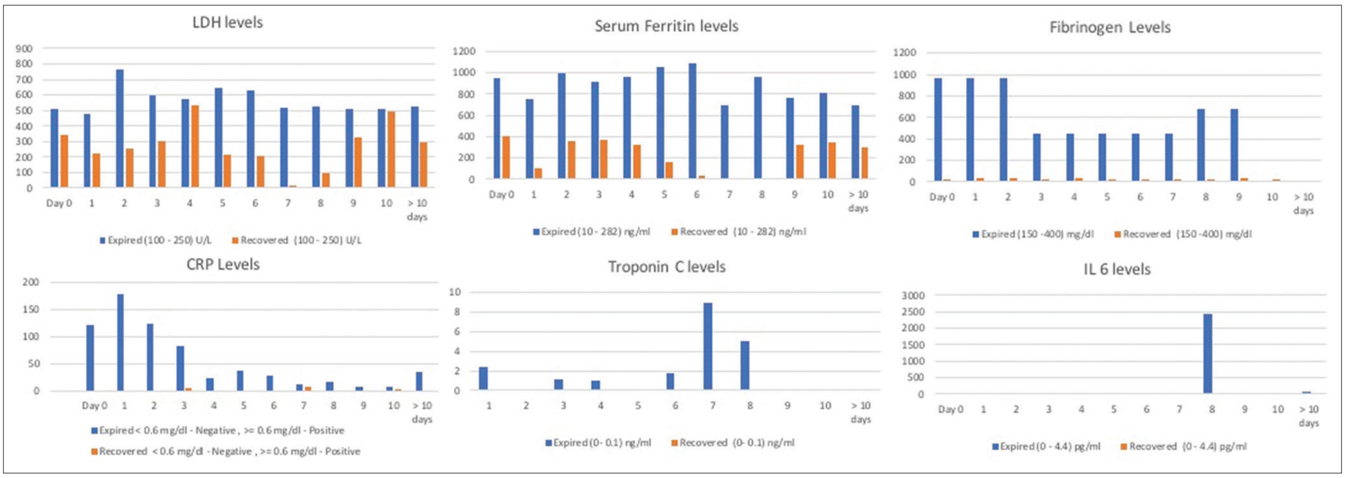

Figure 5: Variation of acute phase reactants. An exponential rise in the levels of serum LDH, serum ferritin, fibrinogen, CRP and IL6 levels was seen in the expired patients

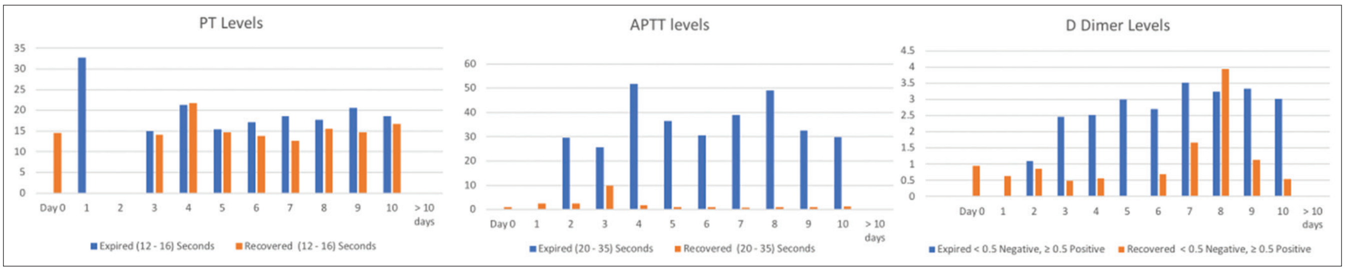

Figure 6: Variation in D-dimer levels and coagulation profile. A Dimer level of >3 was seen early in the disease in the expired patients, along with an increased value of APTT

Various studies observed a falling lymphocyte count with an increasing disease progression,[9,10] more significantly a lymphocyte percentage of less than 5% was associated with a poor prognosis,[11] along with a repletion of lymphocytes as an important factor for recovery.[12]

An expansion of monocyte population in the ICU bound patients was seen[7] which differs from a low monocyte count observed in our study.

Although no studies comparing the variations in the values of RDW and hematocrit in COVID-19 patients were found, RDW variations during other viral diseases (liver failure in HEV)[13] and poor prognostic marker in various diseases was found.[10-12]

There was no significant variation in the platelet levels in various studies.[1,13,14]

Various studies indicate the importance of an acute renal damage and its association with mortality in COVID-19 particularly during the late disease course,[15-21] whereas other studies showed a relatively low incidence of AKI in COVID-19.[22,23]

The liver enzymes were found to be altered in various studies, particularly in severe COVID-19 disease.[24-28]

A transient and mild variation of the liver function tests was mentioned in other studies with no significant relation to disease severity.[29,30]

A higher levels of the acute phase reactants were seen in more severe disease and in the expired patients than the survivors in a large number of studies.[31-38] with a particular emphasis on the association of LDH, and creatinine as the variables most predictive of respiratory failure, whereas maximal IL-6 level showed the strongest association with the need for mechanical ventilation, followed by maximal CRP level.[11,38-41] An analysis of cardiac makers revealed a much higher indicated a higher fatality risk associated with abnormal myocardial parameters.[42]

A higher threshold for D-dimer was found to be associated with an increased risk of pulmonary embolism and other complications in COVID-19 patients.[43-47]

A high admission D-dimer levels, and increasing D-dimer trends associated with a significantly greater risk of all-cause mortality were reported in various studies.[44,48-51]

Limitations of the study

The study was conducted on the patients admitted to the hospital in a relatively small cohort of patients. This might represent the variation of results in a selective patient population who have an access to the medical care.

CONCLUSION

We conclude that a highly significant variation was seen in hematology parameters, renal function tests, acute phase reactants, and the coagulation profile in the expired patients. The parameters showing a significant association with the disease progression include

1. Hematology profile with a high WBC count with rising NLR (>3), reduced LMR (<3) with falling lymphocyte percentage along with a borderline low hematocrit and high RDW
2. A significantly altered renal profile with rising BUN and serum creatinine levels
3. An alteration in the liver functions with lower albumin and total protein levels and rising liver enzymes and serum globulin levels
4. Rising levels of acute phase reactants including serum fibrinogen, CRP, and LDH along with an altered coagulation profile with rising D Dimer levels.

Since the disease shows a variable progression with a sudden worsening of the clinical symptoms, a comprehensive monitoring of the laboratory parameters serves to diagnose and treat the disease progression.

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