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REVIEW ARTICLE

An Overview of Coronavirus COVID-19 with their Pathogenesis and Risk Assessment of the Disease Utilizing Positive Predictive Value of the Clinical and Laboratory Data

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Abstract
COVID-19 has created a devastating pandemic, infecting more than 200 countries in its wake, only sparing Antarctica. The virus dissociates ferrous ion from the porphyrin ring of heme of haemoglobin—thus hampering the oxygen and carbon dioxide exchange in the lung and tissue. The toxic effect of ferrous (Fe^{2+}) ions and carbon dioxide causes lung damage giving rise to severe respiratory distress and an often observed clotting disorder. Serum ferritin level is increased along with the rise of serum LDH, D-dimer, serum IL-6 and cardiac troponin. Associated leukocytosis, occasional lymphocytopenia and radiological changes of the lung are the pathological hallmarks of the disease. All these parameters including other clinical data such as age, fever, gender and associated co-morbidities may be used as a Risk Assessment tool for COVID-19 before the report of real-time polymerase chain reaction (RT PCR) is available. A timely intervention can contribute to rescuing millions from an untimely death.

Keywords COVID-19 · Surface protein · Cytokine · Risk assessment · Lab data

Purpose

Time and Risk Assessment are two valuable factors for the treatment and management of suspicious COVID-19 cases due to the high incidence of "death rate". Before the arrival of RT (Reverse Transcript) PCR (Polymerase Chain Reaction) Test for confirmation of COVID-19, underlying risk of the suspicious patient can be assessed from the Lab and clinical data for the best possible treatment. Thus valuable lives could be saved by giving Interleukin blocker or glucocorticoids earlier and taking proper care of oxygen saturation.

Introduction

The epidemiology of agent, host, environment with bio-clinical characteristics of patients with COVID-19 has been described below:

COVID-19 virus is labeled as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which was previously, referred to as 2019-nCoV. The virus is a positive-strand RNA virus. Its structural proteins include spike glycoprotein (S), envelope small protein (E), membrane protein (M), and nucleocapsid phosphoprotein (N) (Fig. 1) (Fehr and Perlman 2015; Oostra et al. 2020).

Entree of the SARS CoV2 and subsequent change in the host environment are outlined: Researchers noticed that goblet and ciliated cells in the nose and nasopharynx have high levels of the receptor protein—ACE2 (Angiotensin-Converting Enzyme 2) and the TMPRSS2 protease (Trans-Membrane Protease, Serine 2) which can activate SARS-CoV-2 entry into the host cells (Li et al. 2003). The cornea of the eye, the lacrimal duct and the lining of the intestine may be alternative routes of infection (Oostra et al. 2020). After binding with the receptor, the virus enters into the host cell cytosol. The S-protein-receptor interaction is the

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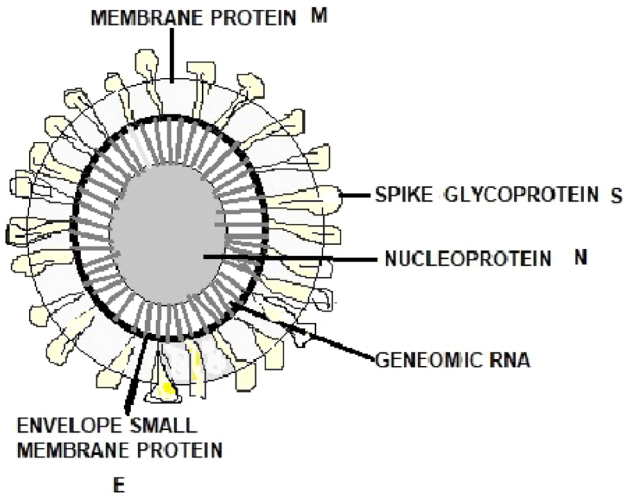


Fig. 1 SARS CoV-2

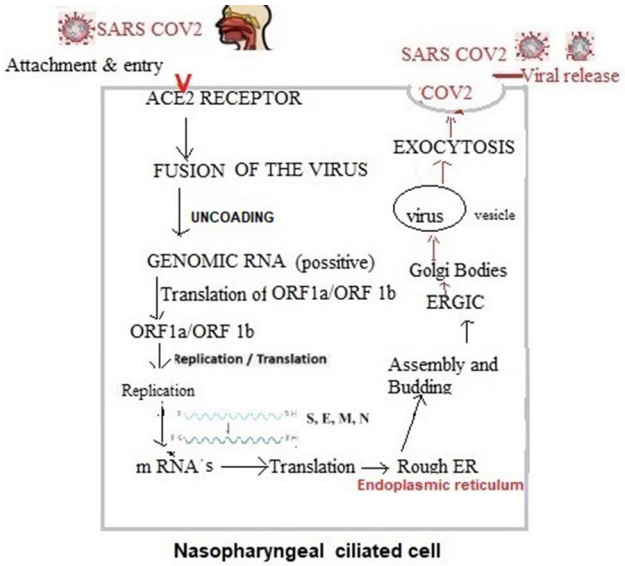


Fig. 2 Entrée of SARS CoV2 and host reaction

primary determinant for the virus to infect a host cell and also directs the tissue tropism of the virus (Fig. 1).

An outline of replication of SARS-CoV-2 is described in Fig. 2: the next step in the SARS CoV-2 or COVID-19 lifecycle is the translation of the replicase gene from the virion genomic RNA. The replicase gene encodes ORFS (Open Reading Frames) (Stertz et al. 2007). SARS-CoV-2 encodes viral proteins up to 14 ORFS. The transcription works through the replication-transcription complex (RCT) organized in double-membrane vesicles and via the synthesis of subgenomic RNAs (sgRNAs) sequences. Following this assembly, budding occurs through rough ER (endoplasmic reticulum) as ERGIC (ER-golgi intermediate compartment) and in the golgi bodies virus replicates and is contained in the vesicle. Finally, by a process of exocytosis release of the virus may occur as early as 3 h after infection. Thus like photocopier machine host cells produce hundreds and thousands of virus for the next kill (Li et al. 2003; Stertz et al. 2007).

Pathogenesis after multiplication is described briefly in Figs. 3 and 4: Next target of attack of the virus is the hemoglobin. Hemoglobin (Hb) of the red blood corpuscle has two components namely Haem and Globin. Haem contains a porphyrin ring. The nitrogen molecules at the center of the porphyn ring are capable of "hosting" an iron molecule (Streitweiser and Heathcock 1981). Fe^{2+} attached with the porphyrin ring of haem is responsible for transport of the oxygen (O_2) and CO_2 in the tissues as Fe-O_2 or Fe-CO_2 complex (Fig. 3).

Viruses that bind to porphyrins (which have two photon of energy) could gain energy through the light-induced method and static virus has become highly dynamic (2020). SARS CoV2 attacks the 1-beta of chain of hemoglobin hijacking this porphyrin ring and dislodging toxic Fe^{2+} ion. This Fe^{2+} ion fails to carry O_2 and CO_2. Due to the lack of O_2/CO_2 exchange in the lung, CO_2 damages lung tissue along with the toxic ion of Fe^{2+} (Fig. 4) (Liu and Li 2020).

IL-6 (Interleukin 6), a multi-functional cytokine (a protein) produced by a range of cells, plays a central role in host defense mechanisms and is involved in the induction of B (lymphocyte) cell differentiation. There will be an accumulation of toxic iron ions, which will increase cytokine and in turn produces hyper-inflammation in the tissue with an increase in the C-reactive protein and albumin (Zandman-Goddard and Shoenfeld 2008; Mehta et al. 2020; Kernan and Carcillo 2017). To combat the increased Fe^{2+} concentration, the release of high serum Ferritin level as a part of immunity system causes a chain reaction with an appreciable change in the values such as high serum LDH (lactate dehydrogenase), low lymphocyte and platelet count and increased white blood cell and neutrophils (Mehta et al. 2020; Kernan and Carcillo 2017). Cytokine regulates ferritin synthesis by initiating the Ferritin regulatory gene, tissue necrosis, factor-alpha and interleukin-1 alpha at different levels (transcriptional, post-transcriptional, translational) during inflammation. Ferritin is a blood protein that combines with the Fe^{2+} ion. During active infection, increased Ferritin level signifies a vital host defense mechanism that attempts to remove viral growth and defends immune cell function (Li et al. 2003). Hyper inflammation due to cytokine produces "Cytokine Storm Syndrome" (Zandman-Goddard and Shoenfeld 2008; Mehta et al. 2020). A cytokine profile is associated with severity of COVID-19 disease, characterized by increased interleukin (IL)-2, IL-6 and granulocyte-colony, increased serum Ferritin, LDH, C Reactive protein, the rise of D-dimer

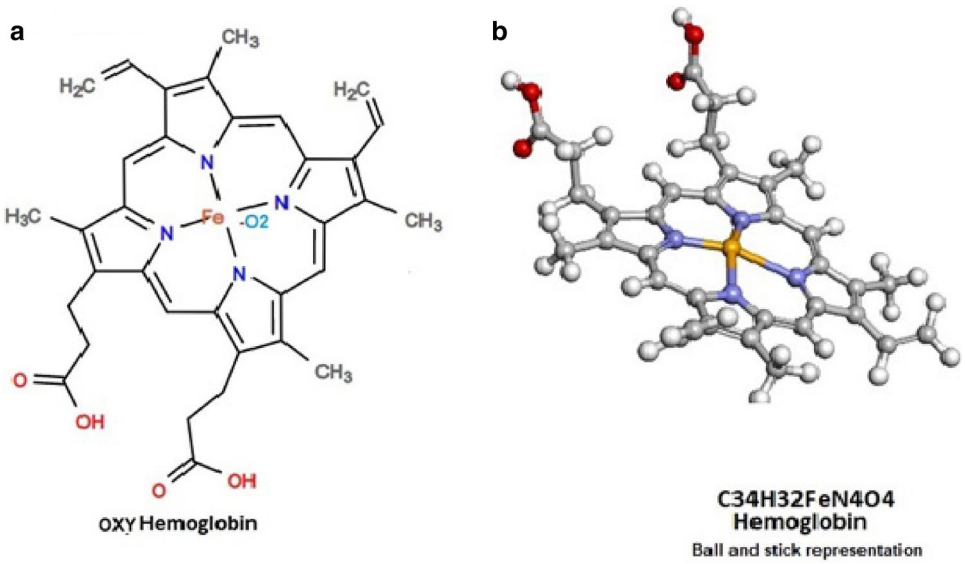


Fig. 3 Hemoglobin (courtesy A Ganguly MRES,MSc)

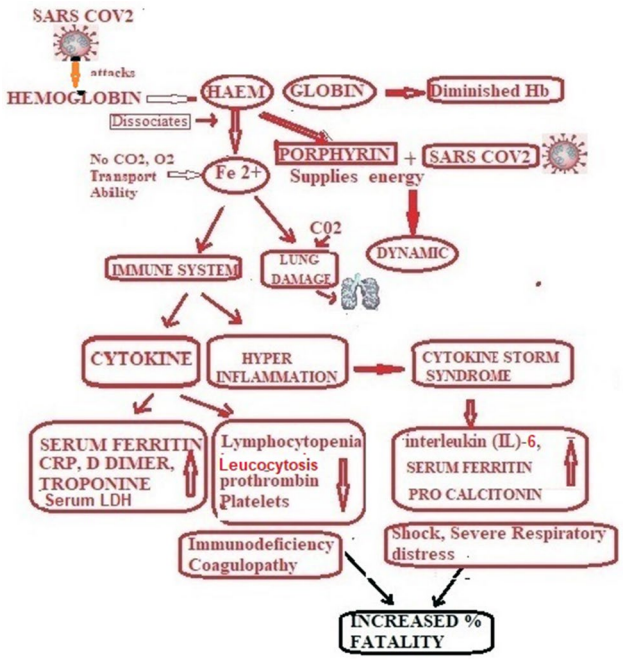


Fig. 4 Pathogenesis

and INR (Li et al. 2003; Stertz et al. 2007). Figure 4 illustrates the schematic outline of the pathogenesis.

Materials and Methods

Laboratory and clinical data of 91 Indian patients (49 patients from hospitals of Kolkata, West Bengal), 21 patients from Jaipur and 21 patients from Delhi and suburbs) were analyzed (Bhandari et al. 2020; Gupta et al. 2020; Rukmini 2020). By the help of Electronic Search engine (Google Scholar) and using NYP-CUIMC clinical data warehouse of Columbia University Irving Medical Center (CUIMC) full text of all the articles were accessed. According to these search criteria our meta analysis included only patients with or without the severe disease who have Lab data (Columbia University Irving Medical Center (CUIMC) 2020; Mehra et al. 2020; Geleris et al. 2020). Hematological and laboratory data of more than 10,000 COVID-19 patients, provided by several American, Italian and French researchers have also been studied (Columbia University Irving Medical Center (CUIMC) 2020; Mehra et al. 2020; Geleris et al. 2020).

Twenty-one COVID-19 positive patients who were admitted in S.M.S Hospital, Jaipur, Rajasthan have been reported by Bhandari et al. (2020). Most of the patients were foreigners from Italy, Spain, USA and UK. Study of twenty-one patients reported by Gupta et al. was included as a study cohort over a period of January–March 2020 in Safdarjanj Hospital, New Delhi. Thirteen (62%) patients had recent travel history outside India in the previous 30 days, two-thirds of whom had travelled to Italy (Gupta et al. 2020). Our sample study has also included the data provided by Mehra et al. of Brigham and Women's Hospital of Harvard Medical School, Boston, USA (Mehra et al. 2020). Out of 8910 patients of COVID-19, 1536 patients (17.2%) hail from North America, 5755 (64.6%) patients from Europe, and 1619 (18.2%) from Asia (Columbia University Irving Medical Center (CUIMC) 2020). Geleris et al. had reported of 1446 consecutive COVID-19 patients of Newyork, USA (Mehra et al. 2020) who had a trial with Hydroxy Chloroquin. Retrospective cohort study of COVID-19 by Giulio Cavalli of 29 patients of the San Raffaele Hospital, a

designated COVID-19, tertiary health-care centre in Milan, Italy was also included (Geleris et al. 2020).

Llitjos et al. (2020) noticed a high rate of thromboembolic events in COVID-19 patients treated with therapeutic anticoagulation, with 56% of Venous thrombo-embolism and 6 pulmonary embolisms out of 26 consecutive patients with severe COVID-19 admitted in two French intensive care units (ICU) from March 19th to April 11th of 2020. Gupta et al. analysed 2245 patients having severe acute respiratory illness (SARI) from 52 districts of 20 states of India out of which there were 104 COVID-19 patients (Gupta et al. 2020). Bhatnagar et al. (2020) studied and reported laboratory status of three patients in Kerala, India and recommended treatment protocol with Lopinivir. 61 patients of Brazil were reported by Nascimento et al. (2020). The data of these patients were compared with the analysis of pooled data of Fei Zhou of China and Giuseppe Lippi and Mario Plebani of Italy who pointed out the blood hematological and laboratory data in the early March of 2020 (Zhou et al. 2020; Lippi and Plebani 2020; Bataille et al. 2020). Finally, results were also compared with the various parameters reported in the WHO (World Health Organisation) web site

Table 1 Factors For PCA

Factors	Critical cases	Non critical cases	*p* value
Age, years	63 to − 76	45–58	< 0.0001
Gender			0.15
Female	31%	40%	
Male	69%	60%	
Comorbidity	67%	40%	0.0010
Hypertension	48%	23%	0.0008
Diabetes	31%	14%	0.0051
Coronary heart disease	24%	1%	< 0.0001
Chronic obstructive lung disease	6%	1%	0.047
Malignancy	0	1%	0.37
Chronic renal disease	4%	0	0.024
Fever (temperature ≥100 °F)	95%	94%	0.94
Cough	76%	82%	0.15
Days of illness	5–15	8–14	0.53
White blood cell count/mL	4–14	5–8	< 0.0001
7500	9%	20%	< 0.0001
75,000–16,000	45%	69%	
> 16,000	46%	11%	
Lymphocyte count, × 10^9 per L	0.5–0.9	0.8–1.5	< 0.0001
< 0.8	76%	26%	< 0.0001
Hemoglobin, g/L	15–138	12	0.30
Platelet count, × 10^9 per L	1.37–1.8	168	< 0.0001
Albumin, g/L	26.5–31.3	30.6–36	< 0.0001
Lactate dehydrogenase, U/L	363–669	219.0–318.0	< 0.0001
> 300	98%	54%	< 0.0001
Interleukin 6 I, pg/mL	5.6–83.1	1.1–6.5	< 0.0001
> 12–1800	46%	1%	< 0.0001
Prothrobin time, s	11.2–13.7	10.4–12.6	0.0004
< 16	87%	197%	0.016
≥ 16	13%	3%	
D-dimer, ng/mL	1.5–21.1	0.3–1.0	< 0.0001
≤ 250	7%	43%	< 0.0001
> 250–1100	11%	36%	
1100–1600	81%	23%	–
Serum ferritin, µg/L	728.9–2000	264.0–921.5	< 0.0001
402–987	44	71%	0.0008
X Ray-CT features: consolidation	74%	53%	0.0065
Ground-glass haze	81%	67%	0.049
Bilateral pulmonary infiltration	83%	72%	0.090

by several Chinese workers after the first outbreak of the disease in China (Table 1) (World Health Organization 2020; Bataille et al. 2020; Centers for Disease Control andPrevention 2020; World Health Organization 2020; Zhou et al. 2020; Gorbalenya et al. 2020). From the various studies following parameters or Risk factors were identified which had an influence on the clinical course (critical or non critical) of COVID-19 patients (Table 1):

Physical factors—gender, age, days of illness.

Comorbidities—hypertension, diabetes, coronary heart disease, chronic obstructive lung disease, carcinoma/malignant disease, chronic kidney disease.

Clinical finding—temperature, cough, dyspnea.

Hematological and biochemical data: absolute total count of leucocyte and lymphocyte, platelets, neutrophil to lymphocyte ratio, INR. Serum ferritin, serum LDH, D-dimer, Interleukin 6, Cardiac Troponin, Imaging Features (Radiology—X-ray and HRCT of thorax).

Statistical evaluation: number of involvements (percentage), respective p and χ^2 (Chi-Square Test) values of various factors were determined by a special Statistical Application tool "XL STAT" (trial version) of ADDINSOFT (France). To reduce the multi-dimensional facets of the variable/factors Principal Component Analysis (PCA) was applied which shows the relationship between factors (such as critical, noncritical, *p* values) and observations (Fig. 5).

Further binary logical regression of the variables (Table 2) was done by XL STAT assigning COVID-19 Positive as "1" and negative case as "0". Summary statistics of the Chi-square test of association evaluates relationships between categorical variables of rows and columns along with goodness of fit statistics (Fig. 6a, b). Artificial Intelligence (AI) with binary logical regression were applied with Y as quantitative variable and X as quantitative and qualitative variables (Fig. 7).

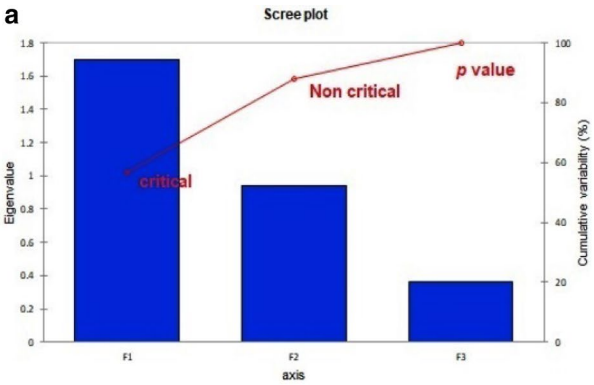
Y/Quantitative Variable: Binary—"0" as COVID-19 negative and "1" as positive—99 rows (observations) and 1 column.

X/Quantitative variables: 99 rows and 10 columns of various variables (factors) of hematological and lab data such as leucocyte, lymphocyte, platelet cell count, NLR (Neutrophil to lymphocyte ratio), INR, serum Ferritin, LDH, D-dimer and Interleukin 6 levels.

X/Qualitative variables: 99 rows and 2 columns of Risk (as low, potential risk, high risk and severely ill condition) and score of the risk was scaled (or graded) as 0–4 (Table 2).

Test of independence between the rows and the columns (Wilks'G2), Wald Chi-square, *p* value, alpha were noted from the statistical analysis along with Test interpretation indicating the Hypothesis (H0) and alternative Hypothesis (Ha) of the relationship between column and rows Test of the null hypothesis along with Goodness of fit statistics of

a



b

Principal Component Analysis:			
Eigenvalues:			
	F1	F2	F3
Eigenvalue	1.701	0.938	0.362
Variability (%)	56.685	31.264	12.051
Cumulative %	56.685	87.949	100.000
Eigenvectors:			
	F1	F2	F3
CRITICAL	0.646	-0.373	-0.666
NON CRITICAL	0.688	-0.095	0.720
p value	0.332	0.923	-0.195

Fig. 5 PCA—Eigenvalue and Eigenvectors

Variables, Comparison of the categories of the qualitative variables (variable COVID-19) was also noted (Fig. 6b).

Preparation of application tool: scoring system after analyzing the interpretation of Logical regression of the variables (Table 2) positive predictive values of different variables or factors were assigned as scoring point system from 0 to 4 in the Excel data sheet (Fig. 8a, b), depending upon the values of the hematological and laboratory data such as leucocyte, lymphocyte cell count, platelet count, neutrophil lymphocyte ratio (NLR), serum ferritin, serum LDH, D-dimer, Interleukin 6 along with findings of Chest X-Ray and CT scan indicating the severity of the disease (Columbia University Irving Medical Center (CUIMC) 2020). Other clinical data (such as age, gender, temperature, respiratory distress) and associated Co-morbidities such as diabetes, heart, lung and kidney disease were considered for indirect added Risk assessment (Fig. 8b). If all these parameters are considered from their Dropdown Value system an accrued value is displayed in the Score Board (Fig. 8a). A high score (>30) would denote severe or critically ill patient.

Table 2 Factors for logistic regression

Covid-19	Score	Risk	Leuco	Lympho	Neutro	Platelet	INR	ng/ml dimer	Serum LDH	SERUM ferritin	Pg/ml IL6	NLR
0	*1*	Low	7500	26	71.5	300,000	0.8	356	120	12	25	2.75
0	*1*	Low	8500	23	74.5	206,000	1	380	165	207	45	3.23
0	*1*	Low	9500	30	67.5	197,000	1.2	400	240	402	65	2.25
0	*1*	Potential	10,500	14	83.5	167,000	1.4	467	260	467	85	5.86
0	*2*	Potential	11,500	15	82.5	155,000	1.6	500	270	500	105	5.5
0	*2*	Potential	12,500	17	80.5	152,000	1.8	656	300	597	125	4.735
1	*3*	High	13,500	18	79.5	65,000	1.2	1100	876	662	145	4.416
1	*3*	High	14,500	20	77.5	36,000	1.4	1150	899	778	165	3.875
1	*3*	High	15,500	19	78.5	106,000	1.6	1200	2100	987	185	4.131
1	*4*	Severe	16,500	21	76.5	70,000	1.8	1300	804	1052	205	3.642
1	*4*	Severe	26,500	22	75.5	100,000	1.91	1400	510	1247	225	3.431
1	*4*	Severe	27,500	21	76.5	80,000	1.34	1600	580	1637	245	3.642
1	*4*	Severe	28,500	21	76.5	36,000	1.34	1670	877	1832	245	3.642
1	*4*	Severe	29,500	17	80.5	80,000	1.34	746	615	1832	245	4.735
1	*4*	Severe	20,500	16	81.5	106,000	1.05	800	615	1832	245	5.093
1	*4*	Severe	21,500	16	81.5	125,000	1.05	656	615	1832	245	5.0937
1	*4*	Severe	22,500	16	81.5	62,000	1.94	656	615	1832	245	5.0937
1	*4*	Severe	23,500	16	81.5	62,000	1.94	656	615	1832	245	5.095
1	*4*	Severe	24,500	16	81.5	62,000	1.94	656	615	1832	245	5.093
1	*4*	Severe	25,500	18	79.5	62,000	1.94	656	615	1832	245	4.4166

Less Critical patients or high risk are marked as 25–30 and potential COVID-19 patients (score of 21 to 24.) General or minimal risk patients would indicate a score of less than 20 points.

Result and discussion

The median Indian deceased patients were older, at 57 yrs, compared to 76 yrs of Italian, Americans, British and Spanish patients (Rukmini 2020). Mandeep et al. (2020) analysed that out of total 8910 patients (80.90%) were below 60 years of age and cases admitted in various hospitals of Boston, 5.8% died in the hospital and 8395 patients survived. Most of the patients in our study cohort and reported by other workers were found to be male (61.40%.) in India (Bhandari et al. 2020). In India, USA, Italy, Spain, France, UK, China showed elevated serum ferritin (1295·6 ng/ml in non-survivors/ critical cases) vs 615·0 ng/ml in survivors / less critical ($p < 0.001$) and InterLeukin-6 > 146 pg/ml ($p < 0.0001$), Serum LDH level 780–2100, D-dimer level rises as high as 1600 ng/ml indicating that fatality may be due to hyper-inflammation initiated by the SARS CoV-2 virus (Fig. 9a, b) (Gupta et al. 2020). Rise of Neutrophil, Leucocyte level occur compared to diminished counts of most patients of china with a significant increase in the values of serum ferritin, erythrocyte sedimentation rate points out the day by day increase or decrease of the hematological or biochemical data level (Bhandari et al. 2020; Gupta et al. 2020; Mehra et al. 2020; Geleris et al. 2020).

Lung Damage—X-Ray Chest or CT Scan Thorax (Fig. 10)—X-Ray is 63% sensitive compared to HRCT (High-Resolution CT) being 82% sensitive. Nodularities and Reticular changes to appear first. Then ground Glass Haze or Crazy Paving. Then Unilateral or Bilateral Consolidation appear (Mehra et al. 2020; Geleris et al. 2020).

Other associated factors such as fever, respiratory distress and cough and Co-morbidities or associated disease such as hypertension, diabetes, coronary arterial disease, and chronic obstructive lung disease aggravate further seriousness of the

a

Goodness of fit statistics (Variable COVID-19):

Statistic	Independent	Full
Observations	159	159
Sum of weights	159.000	159.000
DF	158	146
-2 Log(Likelihood)	37.359	-6.163
R^2(McFadden)	0.000	1.165
R^2(Cox and Snell)	0.000	0.239
R^2(Nagelkerke)	0.000	1.144
AIC	39.359	19.837
SBC	42.428	59.733
Iterations	0	26

Test of the null hypothesis H0: Y=0.975 (Variable COVID-19):

Statistic	DF	Chi-square	Pr > Chi²
-2 Log(Likelihood)	12	43.522	< 0.0001
Score	12	390.237	< 0.0001
Wald	12	12.646	0.395

b

Type II analysis (Variable COVID-19):

		WALD		LR	
Source	DF	Chi-square	Pr > Wald	Chi-square	Pr > LR
LEUCOCYTE	1	0.835	0.361	13.884	0.000
LYMPHOCYTE%	1	1.233	0.267	13.906	0.000
PLATELET	1	0.470	0.493	14.134	0.000
I N R	1	0.709	0.400	14.038	0.000
ng/ml DIMER	1	0.055	0.815	14.101	0.000
SERUM LDH	1	0.661	0.416	14.294	0.000
SERUM FERRITIN	1	1.057	0.304	14.399	0.000
pg/ml IL6	1	0.080	0.778	14.037	0.000
NLR	1	1.574	0.210	13.822	0.000
SCORE	2	2.064	0.356	13.400	0.001
RISK	1	0.086	0.769	13.897	0.000

Hosmer-Lemeshow test (Variable COVID-19):

Statistic	Chi-square	DF	Pr > Chi²
Hosmer-Lemeshow Statis	1.298	1	0.255

Fig. 6 **a** Goodness of fit Statistics and **b** Type II analysis (Variable COVID-19)

disease (Bhandari et al. 2020; Gupta et al. 2020; Mehra et al. 2020).

High-Risk Application tool was applied to hematological and biochemical data of 18 patients of Kolkata who were also tested by real-time RT PCR (Table 3). Three cases showed High-Risk status who were also found COVID-19 positive (Fig. 8a). Other cases showed relatively low score and were tested COVID-19 negative (Fig. 8b). It is seen that the prediction of assessment of Risk of the negative and positive cases were 100% (Fig. 11).

Conclusion

A pandemic caused by COVID-19 has created a devastating condition throughout the world claiming more than 3,70,000 lives so far in about 6 months. Risk assessment Score can predict confidently about the severity of the disease of suspicious COVID-19 infected patients warranting early attention and management before the availability of the RT PCR test for confirmation. Proper treatment and management could prevent early morbidity and death.

Source	Value	Standard erro	Wald Chi-Squar	Pr > Chi²
Intercept	210.589	180.558	1.360	0.243
LEUCOCYTE	0.000	0.000	0.835	0.361
LYMPHOCYTE%	-6.150	5.539	1.233	0.267
NEUTROPHIL%	0.000	0.000		
PLATELET	0.000	0.000	0.470	0.493
I N R	3.631	4.311	0.709	0.400
ng/ml DIMER	0.002	0.008	0.055	0.815
SERUM LDH	-0.004	0.005	0.661	0.416
SERUM FERRITIN	0.009	0.009	1.057	0.304
pg/ml IL6	-0.032	0.112	0.080	0.778
NLR	-23.100	18.411	1.574	0.210
SCORE-1	0.000	0.000		
SCORE-2	-10.400	7.242	2.062	0.151
SCORE-3	0.000	0.000		
SCORE-4	-3.289	6.996	0.221	0.638
RISK-HIGH	0.000	0.000		
RISK-LOW	0.000	0.000		
RISK-POTENTIAL	2.220	7.559	0.086	0.769
RISK-SEVERE	0.000	0.000		

Test of independence between the rows and the columns (Wilks' G^2):	
Wilks' G^2 (Observed value)	95140.674
Wilks' G^2 (Critical value)	1677.704
DF	1584
p-value	< 0.0001
alpha	0.05

:TEST INTERPRETATION :

H0: The rows and the columns of the table are independent.

Ha: There is a link between the rows and the columns of the table.

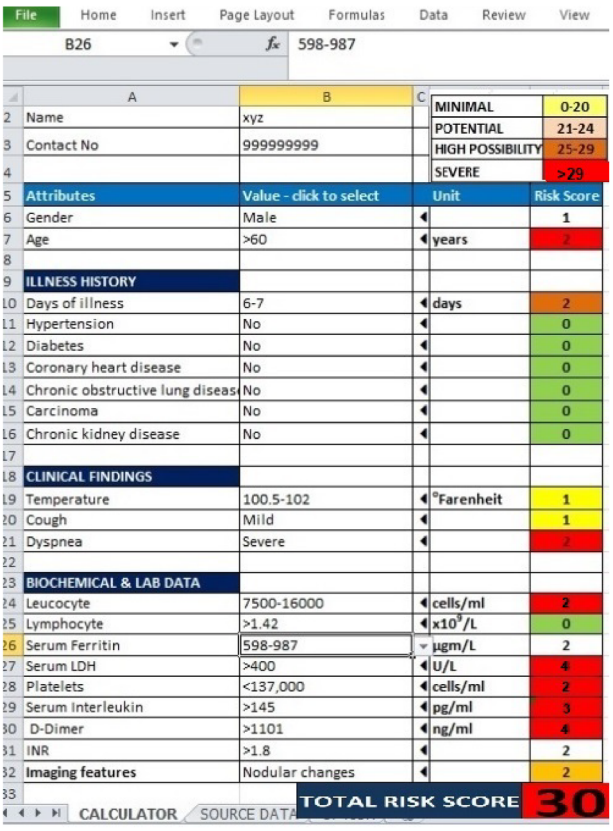
As the computed p-value is lower than the significance level alpha=0.05,

one should reject the null hypothesis H0, and accept the alternative hypothesis Ha.

Summary table:		
	Logistic regression	Random forests
Missclassi	0.025	0.000

Fig. 7 Summary statistics of logistic regression

a



b

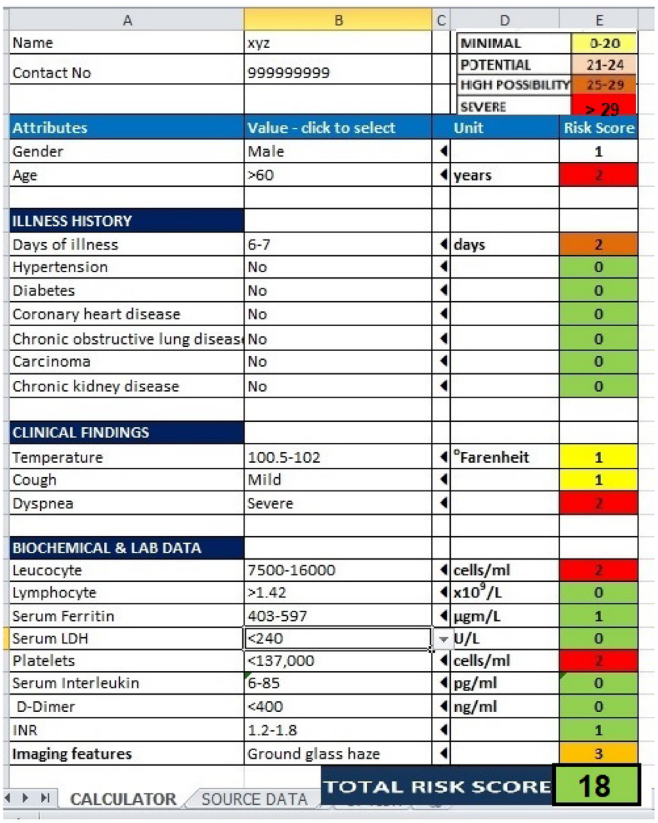


Fig. 8 **a** High risk application. **b** Factors for high risk assessment

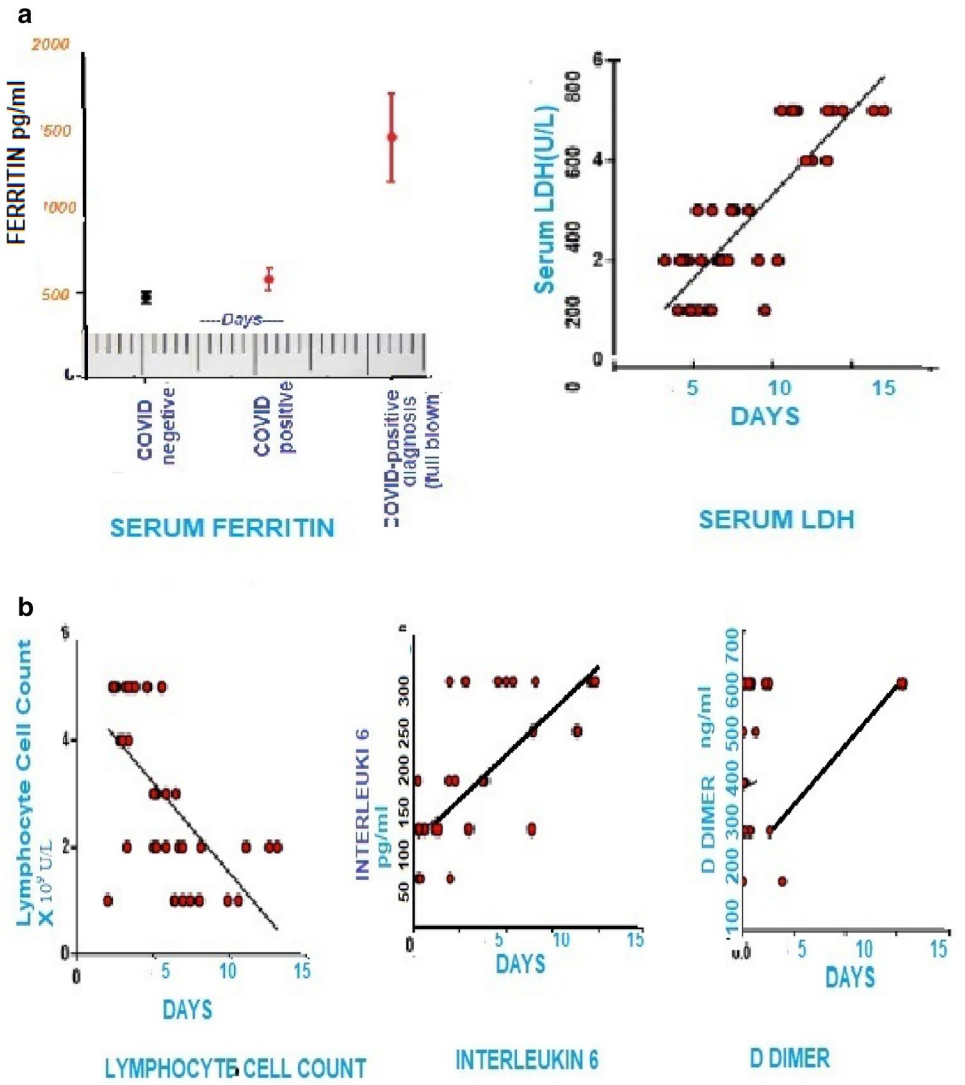


Fig. 9 **a** Biochemical and laboratory data. Serum Ferritin, serum LDH **b** Lymphocyte cell count, Interleikin 6, D-Dimer

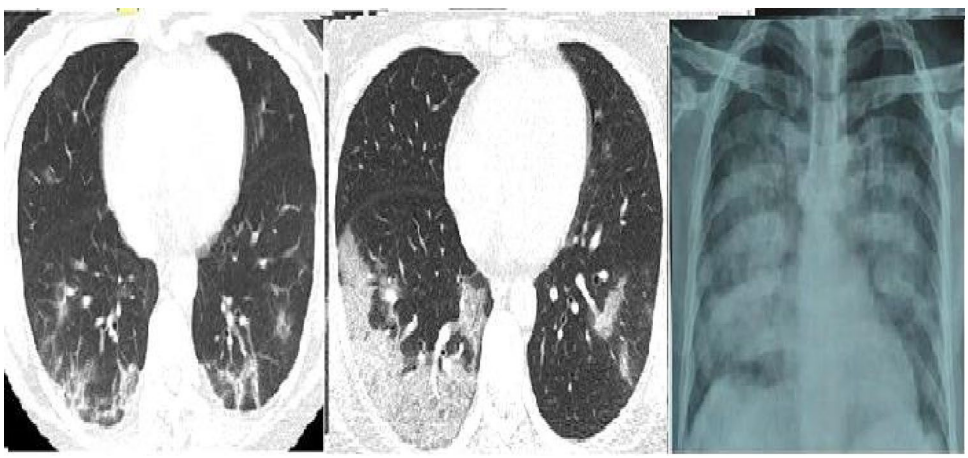


Fig. 10 CT scan of thorax and chest X-ray

Table 3 Data of patients: italics highlighted rows are COVID-19 patients' data

COVID-19	Leuco	Lympho (%)	Neutro (%)	Platelet	INR	ng/mL D-DIME	Serum LDH	Serum ferritin	pg/ml IL6	NLR
PAT1	12,300	22	76	112,000	1.78	746	203	354	130	3.454
PAT2	11,400	27	71	94,000	1.23	356	174	250	124	2.629
PAT3	17,600	19	79	65,000	1.97	1100	450	506	215	4.157
PAT4	13,700	22	76	157,000	1.17	36	150	450	140	3.454
PAT5	10,200	29	69	196,000	1.21	50	122	340	156	2.379
PAT6	21,500	14	84	43,000	1.32	1560	1280	566	130	6.00
PAT7	15,400	24	74	80,000	1.22	89	45	300	145	3.083
PAT8	10,900	32	66	182,000	1.11	90	52	106	45	2.062
PAT9	19,600	21	77	106,000	1.98	523	899	250	74	3.666
PAT10	12,000	33	65	256,000	1.34	360	226	236	87	1.969
PAT11	14,100	39	59	192,000	1.06	300	58	158	100	1.512
PAT12	18,500	21	77	107,000	1.87	304	877	380	25	3.666
PAT13	26,500	16	82	36,000	1.45	1600	2108	358	232	5.125
PAT14	21,600	23	75	86,000	1.96	206	1004	167	134	3.260
PAT15	10,500	25	73	179,000	1.05	4.8	500	176	20	2.92
PAT16	16,700	32	66	211,000	1.23	6.7	210	95	36	2.062
PAT17	11,400	26	72	188,000	1.09	21	167	145	160	2.769
PAT18	8700	28	70	210,000	1.12	4.9	68	100	39	2.500

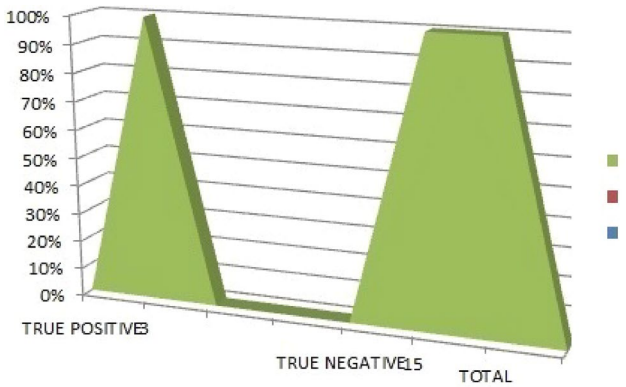


Fig. 11 Prediction of success of interpretation of rate of application tool

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Data availability Availability of data and materials (data transparency): available.

Compliance with ethical standards

Conflicts of interest Completing interests (including appropriate disclosures)—no conflict of interest of the authors.

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