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Can Addressal and Correction of Hematological and Kidney Function Parameters Reduce Mortality in COVID-19?

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ABSTRACT

Background: *Present study was aimed to analyze the difference of hematological parameters and blood urea levels between recovered and dead cases of COVID-19.* ***Material and Methods:*** *A hospital-based study was undertaken wherein hematological parameters and blood urea level of 65 cases were analyzed.* ***Results:*** *Recovered patients, 16 (42.1%) showed higher levels of neutrophils with corresponding 22 (57.9%) patients showing the normal level of lymphocytes, 25 (65.7%) with normal hemoglobin, and 35 (92%) with normal blood urea. On other hand, among 27 died cases, 26 (96.2%) showed higher counts of neutrophils, 1 patient showed normal lymphocytes (3.8%), and 26 (96.2%) with a low count of lymphocytes.* ***Conclusion:*** *Recovery was associated with high counts of lymphocytes, normal hemoglobin, and blood urea levels whereas Mortality was closely associated with deficiency of lymphocytes, low hemoglobin, and high blood urea level. The study suggests supplementation of fresh blood (with live leucocytes) to address the deficiencies and reduce mortalitys.*

Keywords: COVID-19, Hemoglobin, Urea, Mortality, Fresh blood, Coronavirus

INTRODUCTION

Severe Acute Respiratory Syndrome-CoronaVirus-2 (SARS-COV-2) is an ongoing challenge for the health and ultimate survival of the human population. India is currently facing the second wave of pandemics starting from 11th February 2021 embracing 177,108,695 total cases and 3,840,223 total deaths to date i.e. 20th June 2021[1,2].

To reduce case fatality, we need to study carefully, how the recovered and dead cases differ from each other with regards to their vital body function parameters. Although hospital admitted cases of COVID-19 are examined for their vital functions parameters yet the inter-parameter study of vital functionalities does not seem to guide the course of hospital management in the majority of COVID-19 cases.

The present paper reports the comparative account of haematological parameters of recovered and dead cases of

COVID-19 and highlights important observations that the majority of the dead cases were deficient in lymphocyte counts, had low haemoglobin levels, and corresponding high blood urea. The case fatality was associated with a combination of poor immunity, less oxygen combining capacity, and corresponding kidney disease among dead cases. The results of the present study sensitize to investigate further whether addressal and correction of haematological and kidney function parameters, along with ongoing treatment protocols of COVID-19 patients can reduce mortality.

MATERIALS AND METHODS

A study of the association between Kidney Function Tests and haematological parameters and survival/mortality of COVID-19 patients was undertaken among patients reporting in Noida and Greater Noida, UP, India. Surviving and Dead cases were chosen at random for the study. Few investigations were done in the residential society as per the information of COVID-19 patients obtained from the society notifications/news board. Few samples were also studied among students, staff, and faculty in Sharda University who had either been a patient of COVID-19 or had any family members infected with COVID-19 in the past. Some information was collected from the patient's records of Sharda Hospital, Greater Noida, UP, India after obtaining appropriate permission from the hospital administration. The contact details of the COVID-19 patients obtained from the above survey were tabulated and patients were contacted telephonically. The aims and objectives of this study were telephonically conveyed to the patients or their family members (whosoever were available on phone for the conversation). After taking their verbal consent for participation in the study, their kidney function tests parameters were noted down along with other clinical parameters.

RESULTS

Association between Haematological Parameters, Blood Urea level, and Recovery of Patients of COVID-19

The observations on haematological parameters in association with a kidney function parameter, blood urea level was analysed concerning 38 COVID-19 cases who recovered from the disease and 27 cases of died of the disease. In total 65 cases were studied. The age composition of the total 38 patients who were in the category of recovered, ranged from children to old age people. 5.2% were of the age 0-20 (1 female and 1 male), 34.21% were of the age 21-40 years (7 female and 6 male), 26.31% were of the age 41-60 years (5 females and 5 males) and 31.57% were above 61 years of age (2 females and 10 males). The duration of treatment and recovery was observed to be two days' minimum period to a maximum period of 18 days.

It was observed that 16 (42.1%) patients showed higher levels of neutrophils indicating chances of bacterial or fungal infections mixed with SARS CoV-2 infection. Parallel to this, 16 patients also showed low levels of lymphocytes indicating the possibility of a weak immune response against mixed infections.

Out of 38 Recovered patients, 25 (65.7%) had normal values of haemoglobin and only 13 recovered cases (34.21%) were on the margin of being anaemic. Blood urea level among 35 recovered cases (92%) was in the normal range indicating that the majority of recovered patients had normal haemoglobin and blood urea levels (Table 1).

Table 1 Association of haematological parameters and blood urea levels with recovery of patients from COVID-19

S.No	Patient code	Age	Sex	Day of discharge after hospitalization	Neutrophils (%) Reference level: 40%-70%	Lymphocytes (%) Reference level: 20%-45%	Haemoglobin (g/dl) Reference level: 12 gm/dl-15.00 gm/dl	Blood Urea (g/dl) Reference level:20 mg/dl -43.0 mg/dl
1.	SCR 5	41	M	8th	64	25	14.5	38.5
2.	SCR 7	56	F	9th	58	30	11.5	99.7
3.	SCR 9	35	M	10th	50	43	13.7	19.2
4.	SCR 13	62	M	10th	57	33	11.5	30.9
5.	SCR 15	23	F	11th	60	30	10.8	19.2
6.	SCR 16	31	F	10th	60	30	12	16.2
7.	SCR 17	25	F	11th	64	27	9.7	14.8

8.	SCR 18	35	F	9th	60	32	13.2	22
9.	SCR 19	5	F	6th	30	62	11.2	20.5
10.	SCR 20	65	M	8th	58	30	13.2	20.8
11.	SCR 22	37	M	3rd	70	20	14.8	23.1
12.	SCR 25	46	M	8th	67	23	13	24.7
13.	SCR 26	48	F	5th	83	13	13.6	29.7
14.	SCR 27	65	M	14th	90	6	10.3	125.3
15.	SCR90	35	F	7th	40	48	12.6	ND
16.	SCR 28	51	M	7th	71	21	14.5	23.4
17.	SCR 31	78	M	13th	89	6	13.1	61.4
18.	SCR 32	58	F	11th	72	19	12.1	30.4
19.	SCR 35	62	M	8th	57	32	15.5	25.6
20.	SCR 37	65	M	11th	79	13	10	26.5
21.	SCR 38	30	F	7th	81	16	10.5	ND
22.	SCR 41	23	M	7th	46	42	17.7	20.9
23.	SCR 44	23	F	13th	40	50	12	17.5
24.	SCR 45	21	M	13th	43	45	17.1	17.9
25.	SCR 53	59	F	18th	86	8	10.9	35.3
26.	SCR 54	62	M	3rd	59	30	14.3	24.4
27.	SCR 55	74	M	9th	-	30	10.8	40
28.	SCR 56	75	F	8th	86	11	10.2	41.4
29.	SCR 60	52	M	7th	95	3	16.1	82.8
30.	SCR 61	-	F	2nd	60	27	15.9	21.3
31.	SCR 62	41	F	9th	92	6	13.7	40.1
32.	SCR 64	35	M	30th	74	15	13.9	53.1
33.	SCR 65	62	M	4th	85	10	16	34.2
34.	SCR 67	72	F	2nd	78	18	11.5	24.5
35.	SCR 70	68	M	10th	79	11	12.6	ND
36.	SCR 72	14	M	10th	88	10	13.4	25.9
37.	SCR 73	40	M	8th	38	48	14.2	22.9
38.	SCR 74	49	M	12th	94	3	10.1	59.4

Association between Haematological Parameters, Blood Urea level, and Mortality of Patients of COVID-19

We studied a total of 27 patients who died of COVID-19. It was observed that except 1, all the 26 patients (96.2%) who died showed higher levels of neutrophils revealing the possibility of mixed infections. It was interesting to further observe that one of the patients (93.7%) had normal counts of lymphocytes, the cells responsible for imparting adaptive immunity.

Out of 27 Dead cases we studied, as many as 17 (62.9%) showed low levels of haemoglobin, 9 (33.3%) that is around 12-13 gm/dl and only one of the dead patients showed a haemoglobin level of 15.3 gm/dl of blood. Of these patients whose majority showed low haemoglobin, 22 (81.4%) showed a higher level of blood urea.

It was interesting to observe that among 38 patients who recovered of COVID-19 and 27 patients who died, the recovery was associated with high counts of immunity imparting cells lymphocytes, normal haemoglobin, and blood urea levels whereas Mortality was closely associated with deficiency of Immune important lymphocytes, low haemoglobin levels and corresponding high blood urea level (Table 2).

Table 2 Association of haematological parameters and blood urea levels with mortality of patients from COVID-19

S.No	Patient code	Age	Sex	Day of discharge after hospitalization	Neutrophils (%) Reference level: 40%-70%	Lymphocytes (%) Reference level: 20%-45%	Haemoglobin (g/dl) Reference level: 12 gm/dl-15.00 gm/dl	Blood Urea (g/dl) Reference level: 20 mg/dl-43.0 mg/dl
1.	SCD 1	60	M	5th	78	13	9.4	234.9
2.	SCD 2	63	F	6th	92	4	9.4	52.6
3.	SCD 3	80	M	5th	88	5	9.9	86.6
4.	SCD 4	70	M	4th	91	3	7.6	221.8
5.	SCD 5	51	F	3rd	90	7	11.2	39
6.	SCD 7	52	F	8th	93	4	9.2	114.8
7.	SCD 8	24	F	4th	93	6	7.9	63.5
8.	SCD 9	80	F	4th	90	5	12.2	52.4
9.	SCD 10	46	M	6th	89	4	10.5	123.4
10.	SCD 11	63	M	5th	83	8	15.3	116.3
11.	SCD 19	-	M	9th	96	3	12.4	36.1
12.	SCD 21	56	M	2nd	67	31	9.5	ND
13.	SCD 22	67	M	9th	89	7	8.7	29.7
14.	SCD 23	57	F	7th	86	10	10.2	36.3
15.	SCD 24	68	F	2nd	80	15	12	47.8
16.	SCD 28	67	M	5th	90	7	9.6	87
17.	SCD 32	58	M	3rd	90	6	8.7	85.1
18.	SCD 35	71	M	2nd	90	7	11.8	ND
19.	SCD 38	57	M	1st	80	16	12.2	43.2
20.	SCD 42	60	F	2nd	90	6	13.2	67
21.	SCD 52	66	F	7th	93	4	10.3	45.2
22.	SCD 53	66	M	2nd	90	6	13	75.7
23.	SCD 55	40	M	5th	90	5	12.6	42.3
24.	SCD 61	80	M	4th	87	8	11.5	47.7
25.	SCD 62	-	M	8th	88	6	12.6	44.8
26.	SCD 68	-	M	3rd	83	10	12.6	54.3
27.	SCD 69	82	M	3rd	93	3	11.7	133.9

DISCUSSION

The objective of the present study was to analyse how concerning haematological parameters and blood urea level, the two categories of patients, one who recovered and the other who died, differ from each other? In present investigations which were based on the analysis of 65 patients (38 recovered; 27 died), we observed that both recovered, as well as dead patients, showed haematological evidence of mixed infections, yet among patients who died, lymphocytes were below the normal level of counts. Under the circumstances when a mix of bacterial fungal and viral infections is infesting, strong quantitative support of lymphocytes is required to impart innate as well as adaptive immunity. It is well known that among patients of COVID-19 or any other infections, blood is the only medium where either directly through injections or indirectly through oral route medicines against pathogens are given. In addition, due to depleting oxygen saturation levels of lungs, an additional measure of pulmonary oxygen supplementation is taken to bring normalcy and avoid mortality. However, we need an optimum level of haemoglobin to combine with the pulmonary supplementation of oxygen. In the present study, we observed that the majority of the patients who died did

not have a normal level of haemoglobin and the deficiency appeared to induce kidney disease as we observed a higher level of blood urea in the majority of the fatal cases [3]. This can be supported by the fact that anaemia of chronic kidney failure can lead to an increase in plasma concentrations of the catabolites produced during protein metabolism including urea [4,5]. In such patients, the body tissue blood, being aggressively treated by anti-viral and anti-bacterial drugs but not having enough immunity imparting cells and haemoglobin may produce poor clinical results in terms of their survival. Another important understanding to be added to this COVID-19 triggered uremic manifestation is a relapse of aHUS (Atypical Hemolytic Uremic Syndrome) which may lead to activation of the complement system and thereby endothelial damage [6].

Many viruses Like Epstein Barr Virus, Cytomegalovirus, Human Immunodeficiency Virus, Parvovirus, Hepatitis A, C, etc. have been known to be associated with anaemia [7]. Just as there is an association observed between prevalence of anaemia in Community Associated Pneumonia (CAP), similarly in COVID-19 also, the occurrence of anaemia has been reported but its exact pathogenesis is not known/described [8,9]. And anaemia is known to arise early in the start of kidney disease leading to worsening of the kidney parameters due to reduction/deficiency of erythropoietin production (which is required for the production of RBCs) [3,10-13]. Malnutrition and deficiencies of iron, folate and vitamin B_{12} have also been found to cause a reduction in Hb concentrations [14]. Besides the contribution of viral and other above said factors in anaemic like condition, administration of Ivermectin may also contribute to further worsen the extent of anaemia as the side effects of the drug with few other side effects *viz*; decreased Total leucocyte count, eosinophilia, and abdominal distention, etc. [15,16]. A recent study has of COVID-19 patients has shown that Ivermectin damages the intestinal tissues at a dose of 0.22-170 mg/body weight and recovery was slow and observed only after 14-21 days, necessitating prolonged hospitalization of patients [17].

Recommendations

Thus it appears more than necessary that we consider few additions to the ongoing treatment protocol of COVID-19 patients to reduce mortality. Currently, supplemental oxygen therapy like Low and High Flow Nasal Cannula (LFNC and HFNC), Non-invasive ventilation, etc. are being used for reverting the hypoxia occurring at the lung tissue level. Through this paper, we wish to propose the inclusion of fresh blood infusion (blood taken from healthy donors) which will contain both, live leucocytes to generate an innate and specific immune response and will also serve to supplement haemoglobin. On the other hand, if managing the anaemia occurring at the kidney level is required, then Erythropoietin Stimulating Agent (ESA) may be recommended [18]. Another important recommendation to be added is the identification and management of Haemolytic Uremic Syndrome (through its marker C5b-9) and the use of Complement blockade drugs if required [19,20].

CONCLUSION

The present paper highlights understanding and minutely observing the various COVID-19 patients such that targeted course of action be advised to individual patients.

DECLARATIONS

Conflicts of Interest

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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