Evaluation of regulatory T-cells in SARS-CoV2-infected hemodialysis patients: clinical and radiological correlations

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Background

› Aging Dis. 2021 Oct 1;12(7):1545-1553. doi: 10.14336/AD.2021.0709. eCollection 2021 Oct.

Regulatory T cells in COVID-19

Huan Wang [1], Zhao Wang [1], Wen Cao [1], Qianqian Wu [1], Yujia Yuan [1], Xiangjian Zhang [1 2 3]

Regulatory T cells are an important subpopulation of T cells that exert immunosuppressive effects.

Tregs is significantly reduced in COVID-19 patients, and this reduction may affect COVID-19 patients on several aspects, such as weakening the effect of inflammatory inhibition, causing an imbalance in Treg/Th17 ratio, and increasing the risk of respiratory failure.

Background

The role of $CD4^+$ $FoxP3^+$ regulatory T cells in the immunopathogenesis of COVID-19: implications for treatment

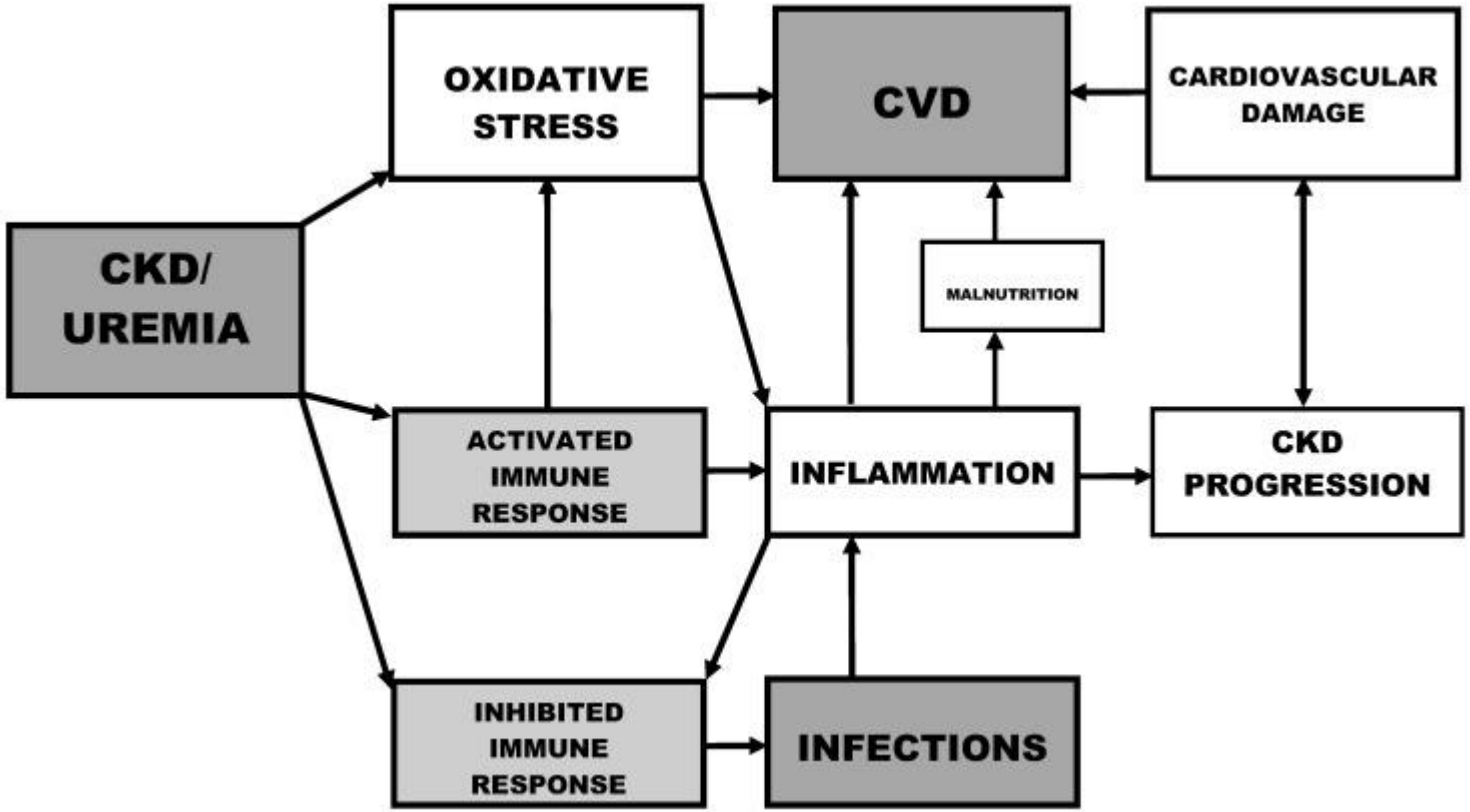
Yifei Wang [1], Jingbin Zheng [1], Md Sahidul Islam [1], Yang Yang [1], Yuanjia Hu [1], Xin Chen [1]

There is an emerging concept of Treg-targeted therapies, including both adoptive Treg transfer and low dose of IL-2 treatment

The potential Treg-boosting effect of therapeutic agents used in the treatment of COVID-19, including dexamethasone, vitamin D, tocilizumab and sarilumab, chloroquine, hydroxychloroquine, azithromycin, adalimumab and tetrandrine should be studied

Hemodialysis Patients

- No data on the T cell response to SARS-CoV-2 in hemodialysis patients are currently available
- Accumulation of uremic toxins was reported to be related to an impaired or dysregulated immune response; both innate and adaptive immunity



Hemodialysis patients

Artif Organs. 2021 May;45(5):E101-E112. doi: 10.1111/aor.13864. Epub 2020 Dec 26.

Continuous renal replacement therapy with the addition of CytoSorb cartridge in critically ill patients with COVID-19 plus acute kidney injury: A case-series

Abdulrahman Alharthy [1], Fahad Faqihi [1], Ziad A Memish [2], Abdullah Balhamar [1], Nasir Nasim [1], Ahmad Shahzad [1], Hani Tamim [3], Saleh A Alqahtani [4], Peter G Brindley [5], Dimitrios Karakitsos [1 6]

Hemodialysis patients

BIOSCIENCE REPORTS

PORTLAND PRESS

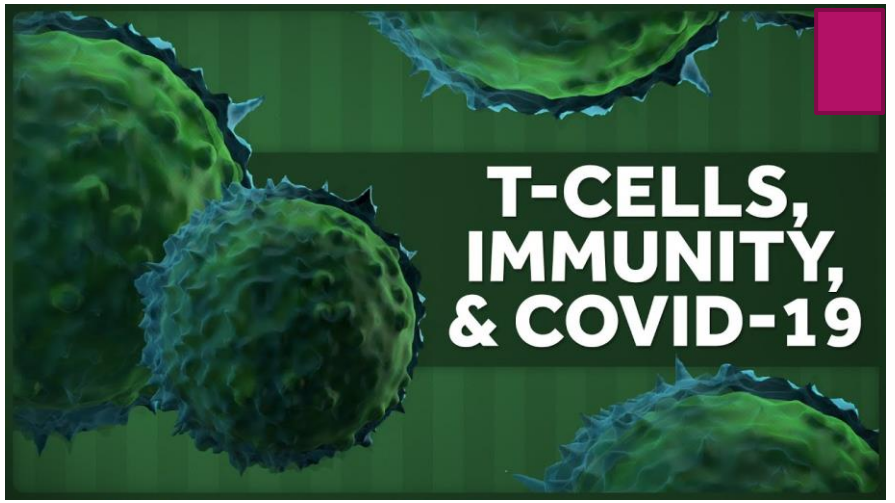
Biosci Rep. 2019 Oct 30; 39(10): BSR20191585.
Published online 2019 Oct 11. doi: 10.1042/BSR20191585

PMCID: PMC6822497
PMID: 31427482

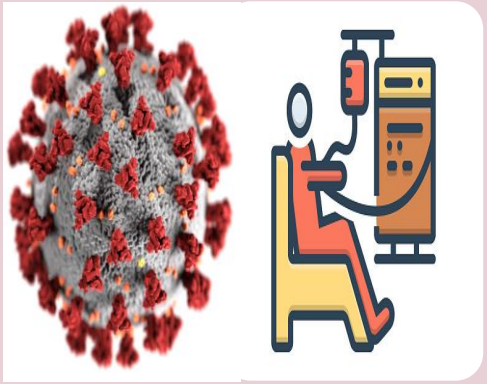
Imbalance of Th22/Treg cells causes microinflammation in uremic patients undergoing hemodialysis

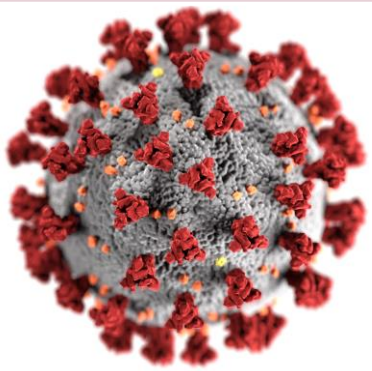
Tingting Ren, Jingyuan Xiong, Guangliang Liu, Shaoyong Wang, Zhongqi Tan, Bin Fu, Ruilin Zhang, Xuesong Liao, Qirong Wang, and Zonglin Guo

- **Tregs have been found to be remarkably decreased in hemodialysis patients before the pandemic of COVID-19**



Our **AIM** was to characterize Treg expression patterns in COV-HD patients and its relation to clinical and radiological severity





30 COV-HD	30 COV	40 HD

REPORTED

Clinical DATA

- Oxygen saturation at admission
- Duration of hospital stay
- In-hospital Mortality
- OPC- Ward- ICU
- Co-morbidities

Radiological DATA

- CORAD score in CT
- Total Severity Score in CT
- Percentage of GGO

Bloods

- Differential Leucocytic Counts
- Neutrophil to Lymphocyte ratio
- D-dimer test
- FCM Analysis

REPORTED (our strength points)

Clinical DATA

Radiological DATA

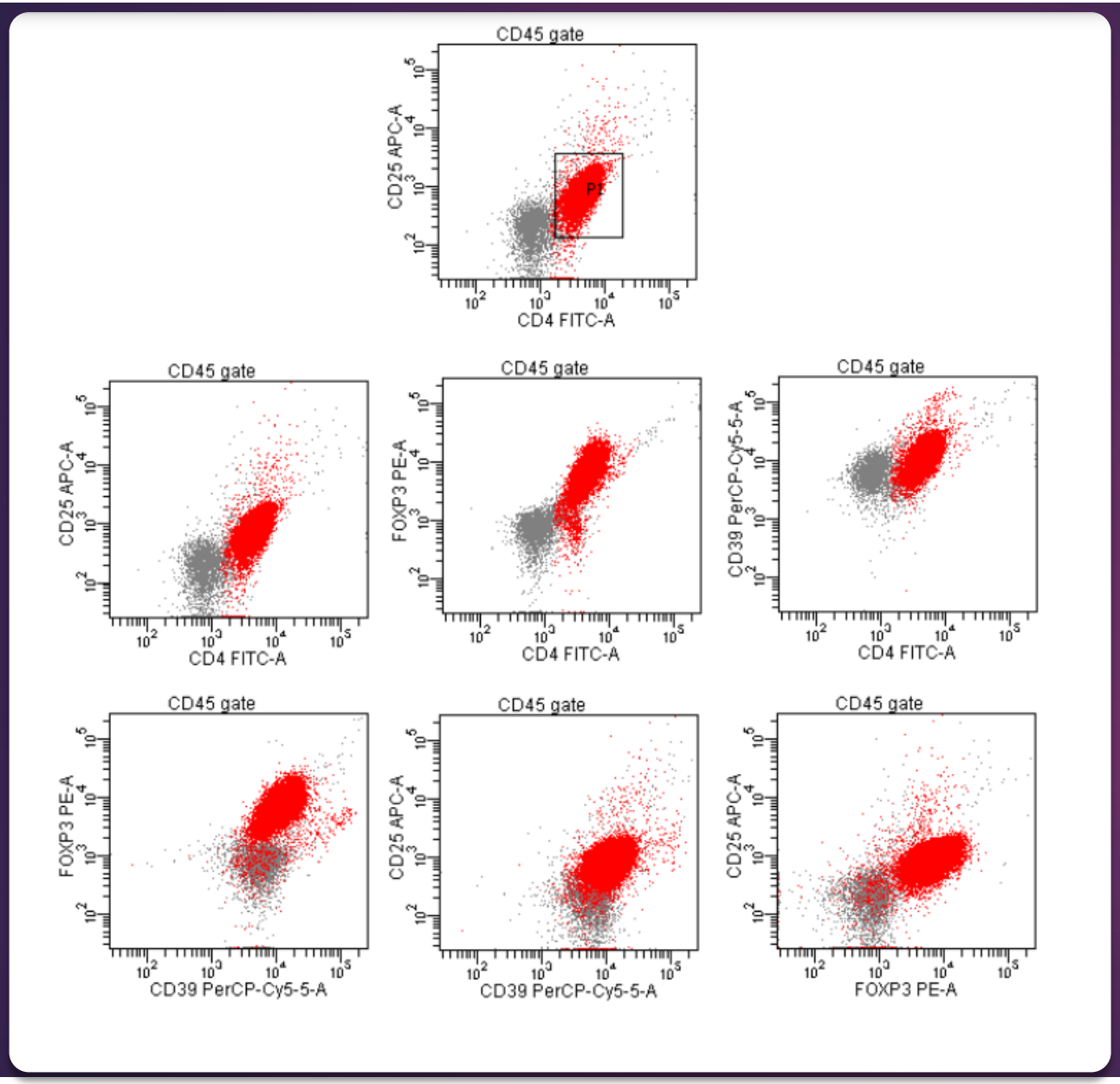
- **Total Severity Score in CT**

Bloods

- **FCM Analysis**

TSS score in CT chest

- five lobes of lungs were assessed for ground-glass opacities, mixed ground-glass opacities, or consolidation.
- Each lobe given 0 to 4 points, depending on the percentage of the involved lobe



FCM Analysis

Main Results (1- All COV versus HD)

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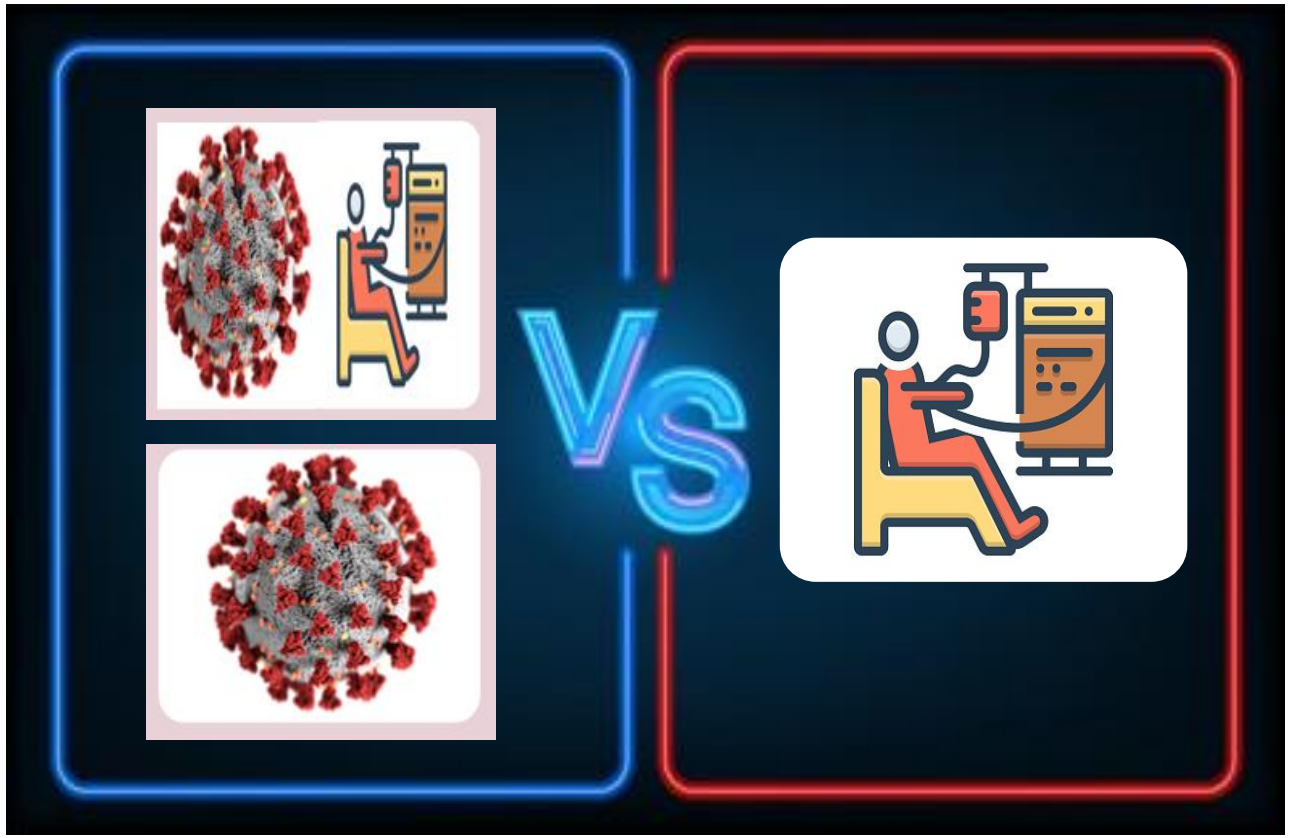

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Comparison between demographic and laboratory data between all Cases of COVID (COV-HD+ COV groups) and control (HD group)				
		Case (COV-HD+ COV groups)	Control (HD group)	P Value
Number		60	40	
Gender	Male	30 (50)	17 (42.5%)	0.54 [a]
	Female	30 (50)	23 (57.5%)	
CBC differential counts				
Total WBCs (cell/ µl)		7600 (3200-22500)	6350 (2300-10200)	**0.02** [a]
Neutrophil (cell/ µl)		5402 (2080-18225)	3270 (782-6796)	**<0.001** [a]
Lymphocyte (cell/ µl)		1137 (480-5000)	1722 (665-3276)	**0.002** [a]
NL ratio (%)		3.44 (1.44-21.7)	1.88 (0.7- 4.99)	**<0.001** [a]
Flowcytometry Analysis				
CD4+ T cells (cell/ µl)		45.1 (1.9-397.6)	125.2 (7.36-1162.9)	**0.001** [a]
T regs (cell/ µl)		0.016 (0- 5.77)	0.28 (0- 140.9)	**<0.001** [a]

Main Results (2- COV-HD versus COV)

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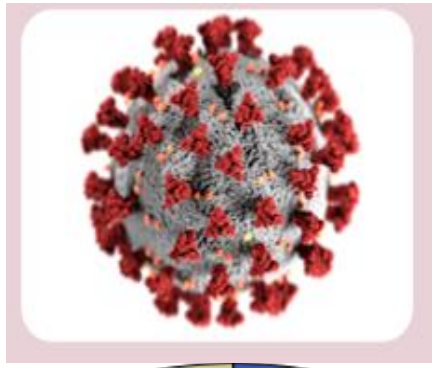
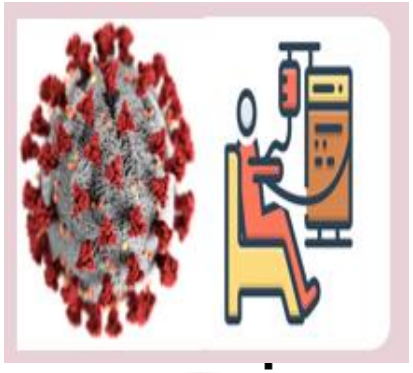
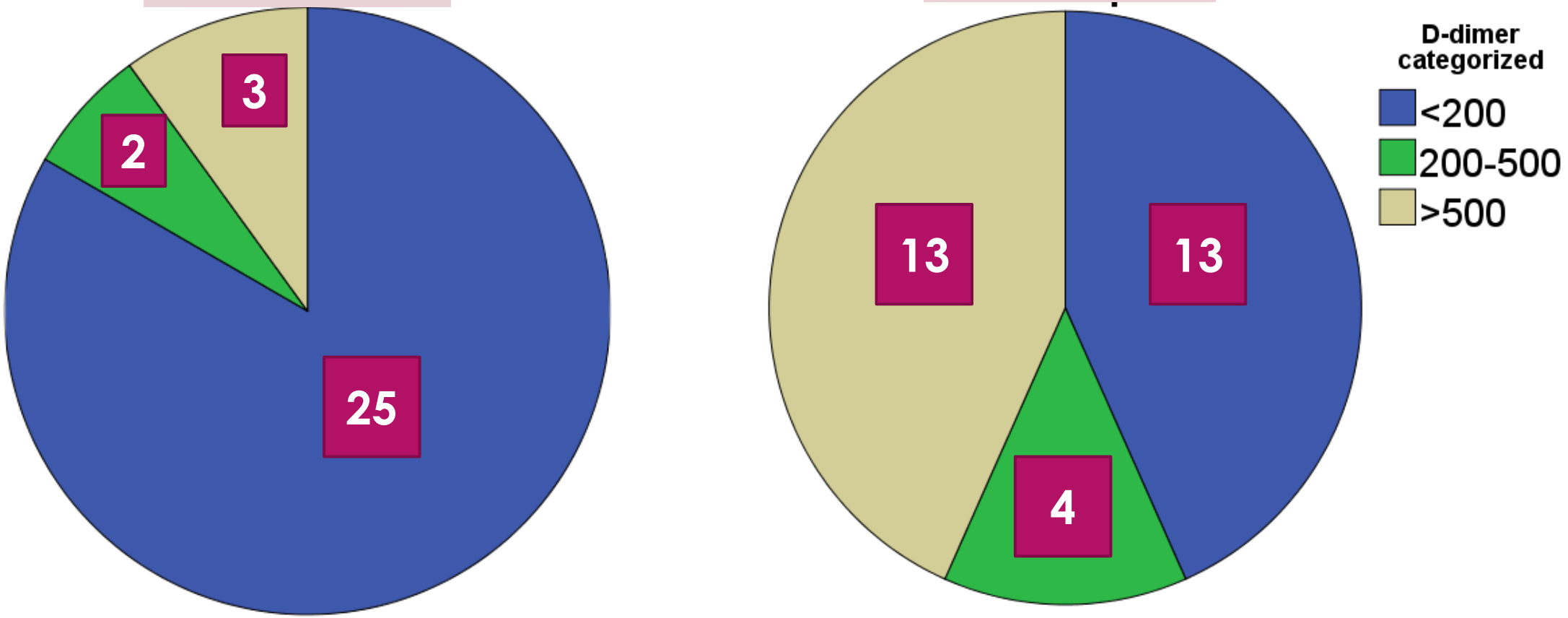
Comparison between demographic, clinical, laboratory, and radiological between all SARS-COV2 infected groups			
	COV group	COV-HD group	P value
Demographic and Clinical data			
Number	30	30	
Age	60.6 (13.6)	54 (8.9)	0.115 [a]
Diabetes	14 (46.7)	13 (43)	0.5
Radiological Data			
GGO percentage%	50 (0- 86)	45 (0- 69)	0.19 [a]
Total severity score in CT (TSS) (out of 20)	7.5 (2- 15)	7 (2- 15)	0.12 [a]
Laboratory data CBC and Coagulation			
Total WBCs (cell/ µl)	8616 (3200-20800)	7300 (3560- 22500)	0.423[a]
Neutrophil (cell/ µl)	6790 (2080-14890)	4346 (2242-18225)	0.152 [a]
Lymphocyte (cell/ µl)	1100 (500-3600)	1204 (480-5000)	0.9 [a]
NL ratio	5.6 (1.81- 13.22)	2.8 (1.84-21.75)	0.132 [a]
Flowcytometry Data			
CD4+ T cells (cell/ µl)	33.8 (2.2- 359.1)	52.16 (1.92-399.6)	0.4 [a]
T reg cells (cell/ µl)	0.011 (0- 0.33)	0.028 (0-5.77)	0.1 [a]

No significant differences







The only Laboratory difference was in D-dimer levels at admission

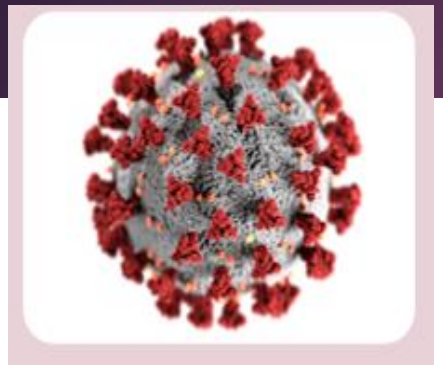
P Value 0.04

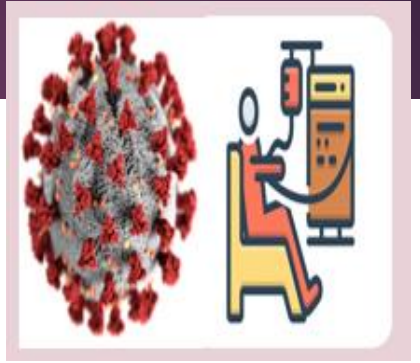
Conclusion 1

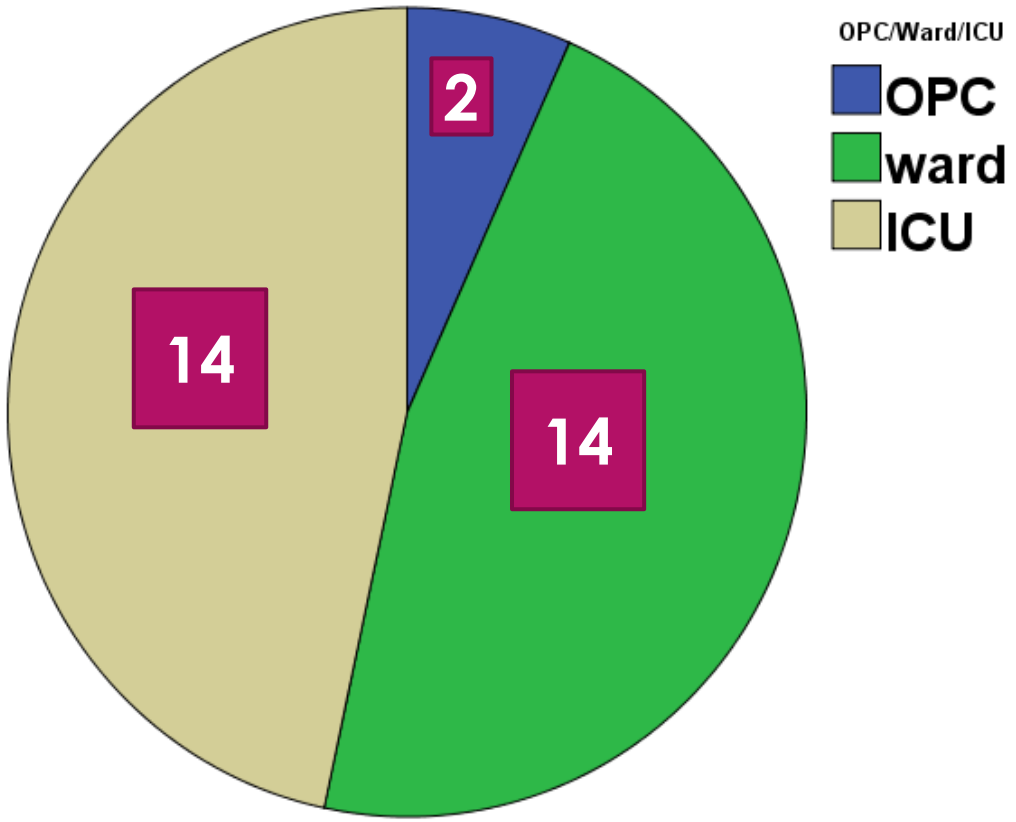
The present study showed significantly decreased CD4+ and T reg cells in patients with COVID-19 whether maintained on HD or not. This suggests that these observed alterations resulted from a SARS-COV-2 effect rather than a HD effect.

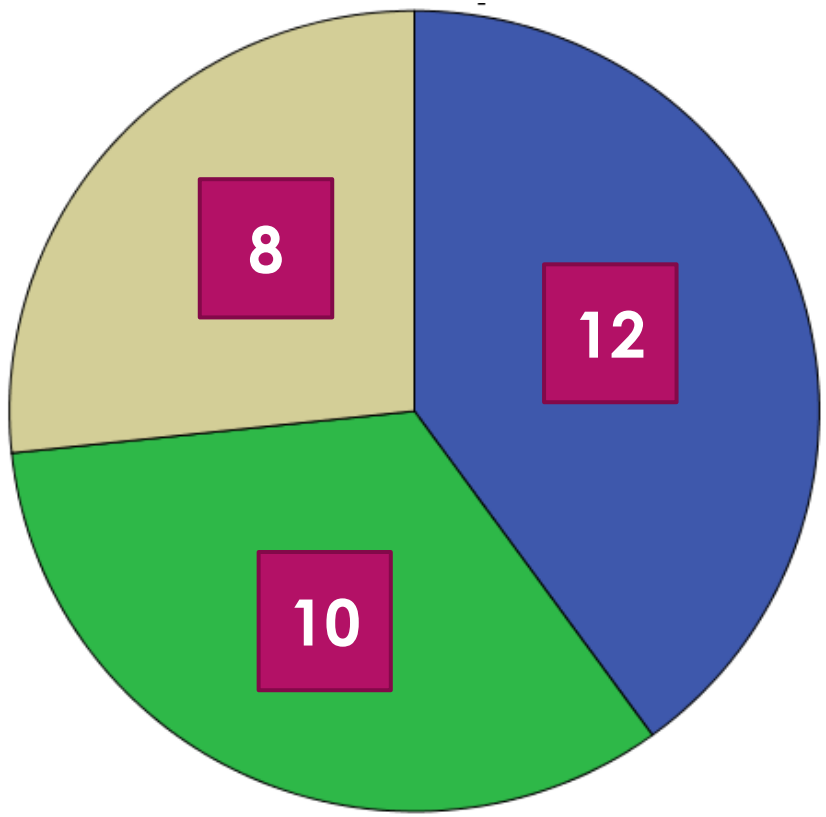
Different Outcomes Despite these comparable clinical data

Age
Comorbidities
Radiological severity
Total and differential WBCs counts
CD4+ and T reg cell counts



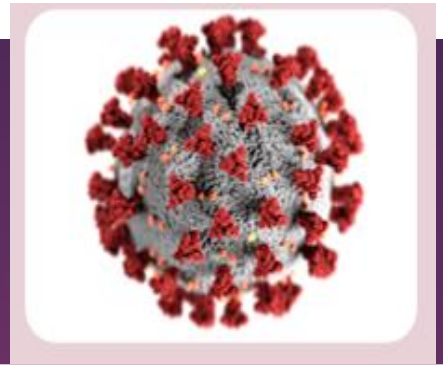






ICU Admission

P Value <0.01



		COV group	COV-HD group	P value
Number of days of hospital admission		15 (3-33)	3 (0-12)	**0.001** [a]
O2 Saturation at admission		88 (60- 99)	89 (72- 96)	**0.008** [a]
Outcome	Discharged for follow-up	16 (53.3%)	12 (40)	**0.005**[c]
	In-Hospital Mortality	13 (43.3%)	7 (23.5%)	

Hospital stay, Hypoxemia, and Mortality

Conclusion 2

The present study demonstrated better survival rates in the COV-HD group compared to the COV group, this may be attributed to

1- More frequent cytokine clearance in regular HD sessions

2- The immune dysregulation and premature aging of T cells in uremic patients

3- Lessened severity indices of patients included in the COV HD group that not met statistical significance in the study sample size

Main Results (3- Correlations)

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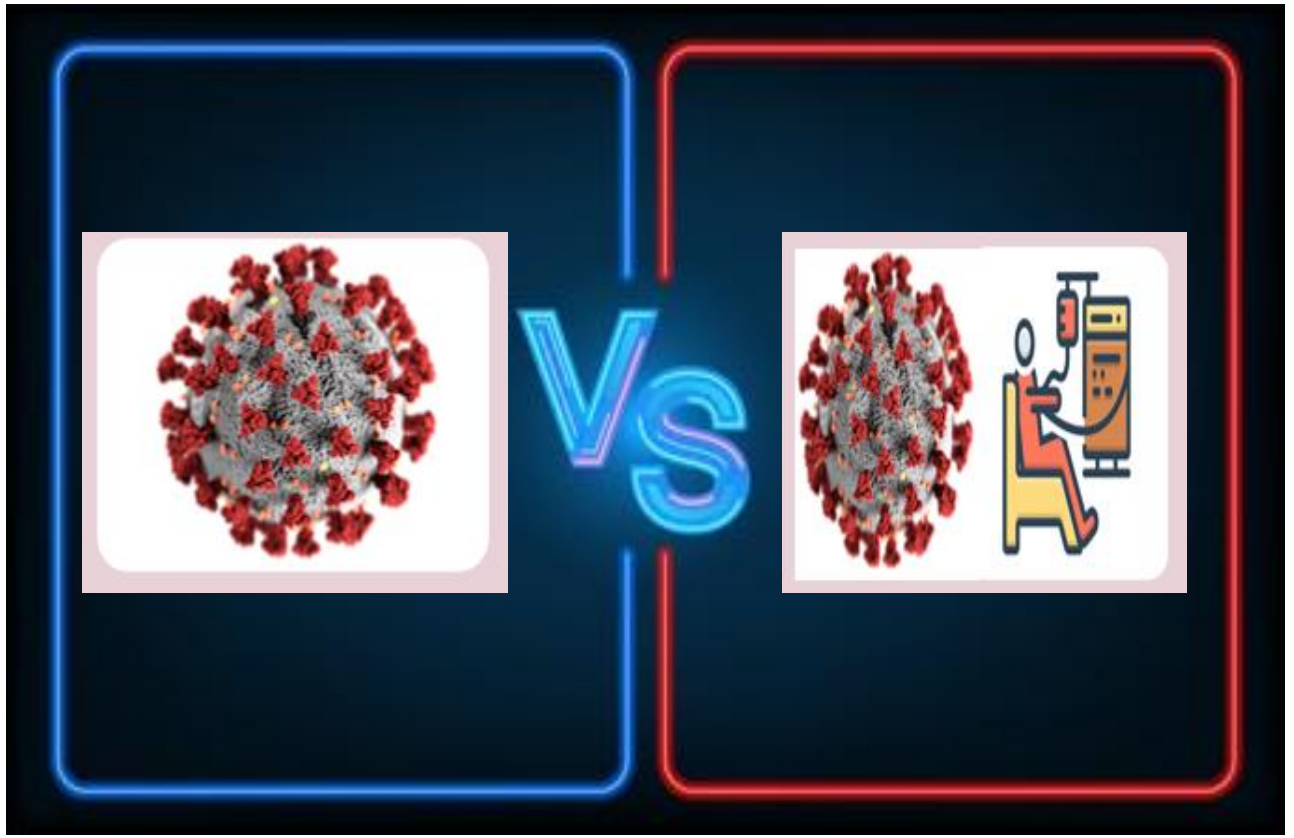

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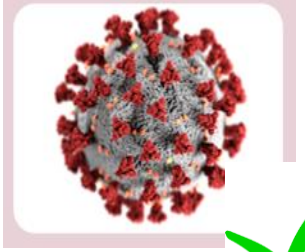
CD4+ T and T reg cell count were tested for correlation to the clinical and radiological severity scores

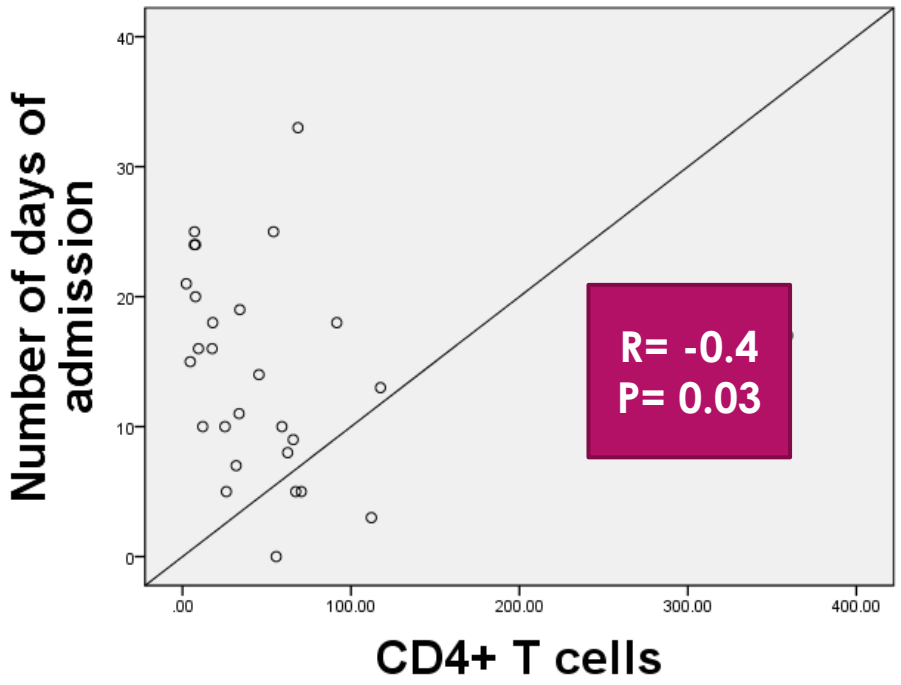
Clinical Severity Criteria

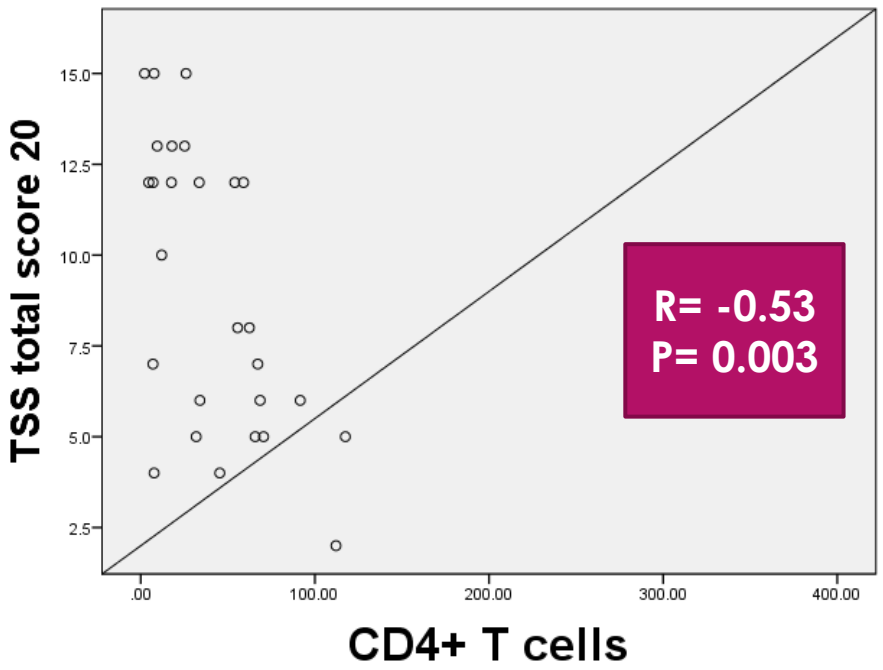
- **Hypoxemia**
- **Number of days of hospital admission**
- **ICU admission**
- **In-Hospital Mortality**

Radiological Severity Criteria

- **Total Severity score in CT**
- **Percentage of GGO in CT**

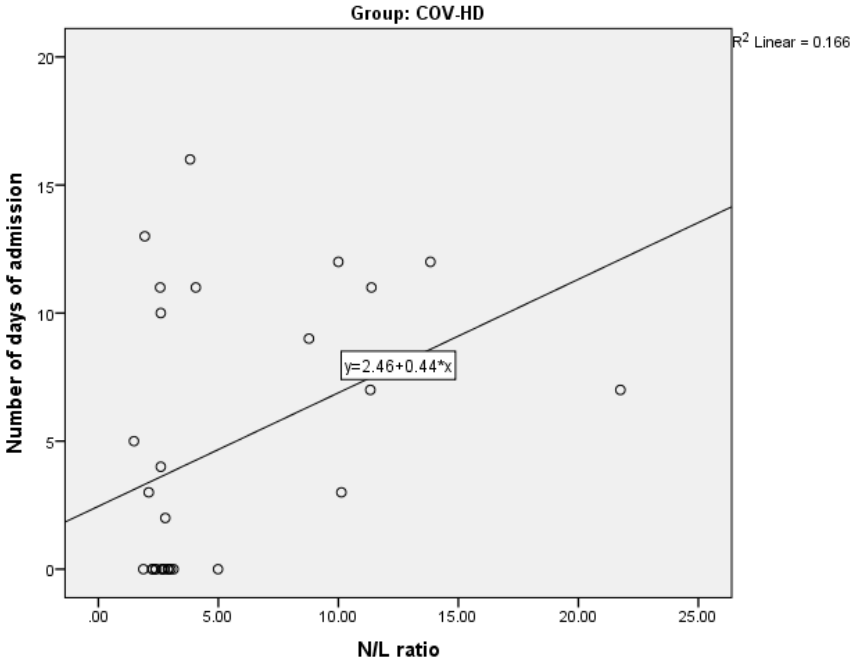


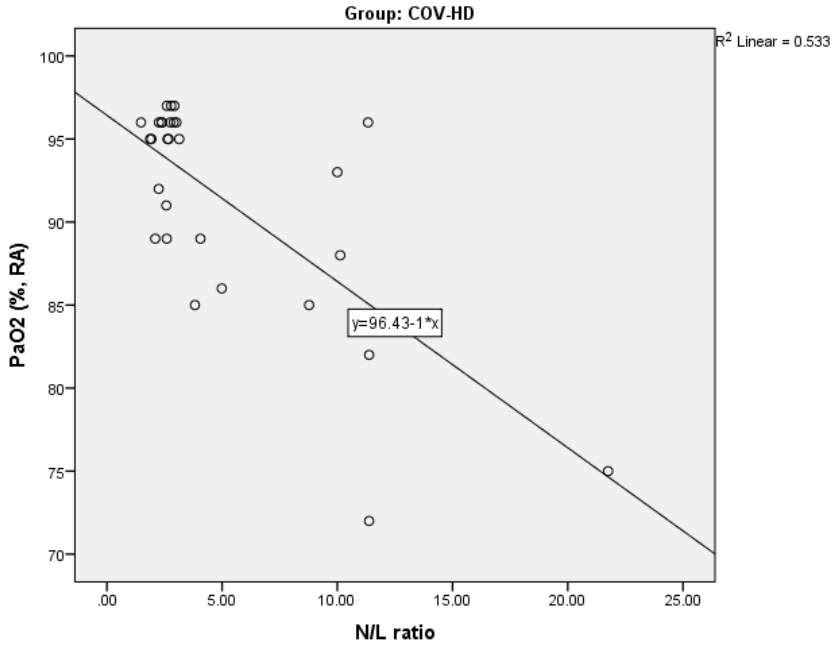


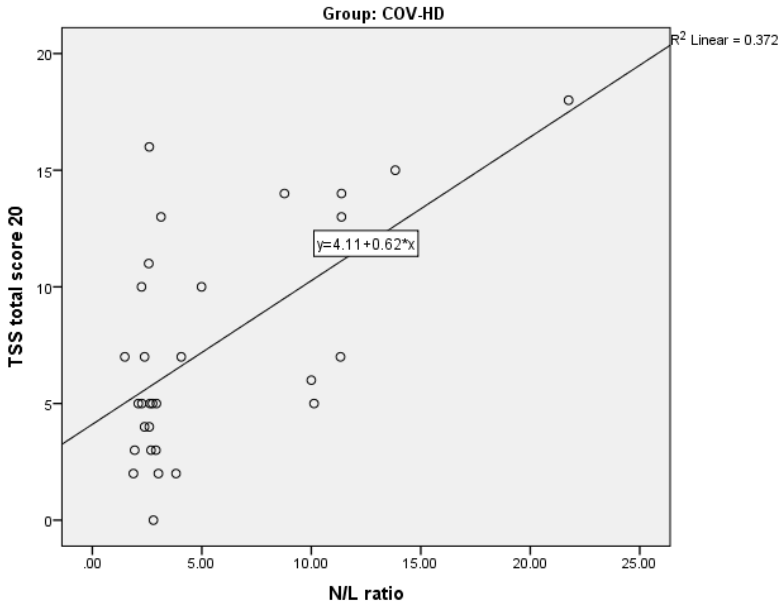


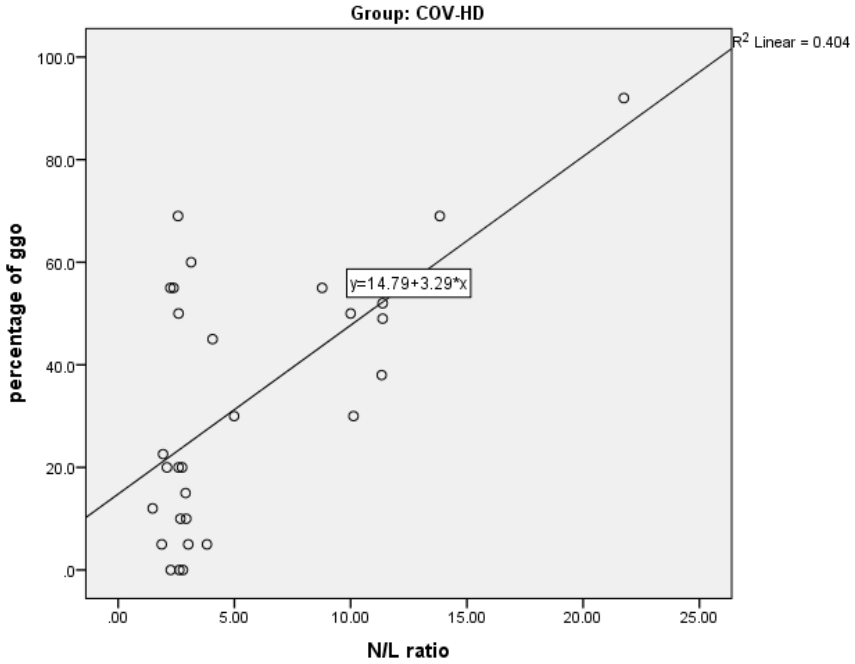
Negative correlation between CD4+ cell count and in-hospital mortality in COV patients
R= -0.54
P= 0.003

The significant negative correlations were reported only in COV group with CD4+ and did not apply to COV-HD group





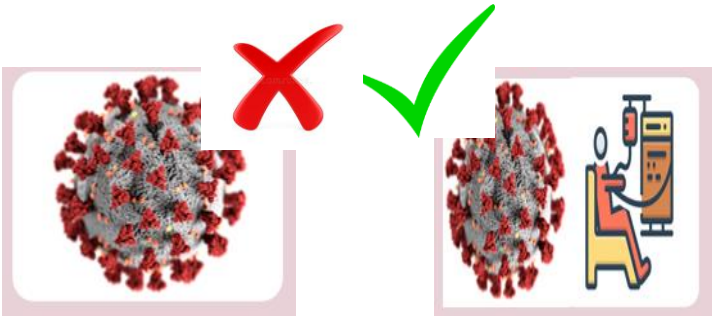




Positive correlation between NLR cell count and in-hospital mortality in COV-HD patients

R=0.71[s]

P <0.001[s]



Conclusion 3

- CD4+ cell counts are negatively correlated with clinical severity outcomes in COV patients and not in COV-HD
- NLR is strongly correlated with clinical severity outcomes in COV-HD patients and not in COV
- T reg cell counts are not correlated to any radiological or clinical severity parameter

Summary and Recommendations

- Our study is the first to evaluate the effect of hemodialysis on T-regulatory cell in SARS-COV-2 infected patients, provide an evidence of T-cell, particularly T-regulatory cell decline in hemodialysis patients with COVID-19, and suggest that hemodialysis per se does not distinctively impact the T-cell response in patients with COVID-19. Therefore, the T-cell targeted therapies for COVID-19 in the general population may be effectively used in hemodialysis patients.

Team Members

Team (Mansoura Faculty of Medicine Staff Members)

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Thank you

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