Section: Medicine

Original Research Article

STUDY OF CORRELATION BETWEEN PROGNOSTIC NUTRITIONAL INDEX (PNI) AND SHORT TERM CLINICAL OUTCOME IN HOSPITALIZED COVID -19 PATIENTS

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ABSTRACT

Background: Objective: To Study of correlation between Prognostic nutritional index (PNI) and short term clinical outcome in hospitalized covid -19 patients.

Material and Methods: All consecutive patients with Age >18 years and RT-PCR diagnosed cases of COVID-19 pneumonia were studied. Prognostic nutritional index (PNI) was calculated on Day 1 of admission using formula: PNI = [(10 × serum albumin (g/dL)) + (0.005 × total lymphocyte count/□l)]17,18. PNI was recalculated on Day 14 if patient stayed for period longer than 14 days. Severity of COVID-19 was established using ICMR criteria. The Ct values of PCR refer to amount of cycles required for the fluorescent signal to exceed background levels. In case of more target DNA, amplification is fast and fewer cycles are required (low Ct value) while for low amount of target DNA more cycles before the fluorescence (higher Ct value). Contact tracers also utilizes Ct values to prioritize their attention to patients with the highest viral genomic load, which indicates a high risk for transmissibility.

Results: Out of 80 patients PNI score was >50 in majority of cases (68.8%) who were considered as normal. Malnourishment was observed in 25 (31.3%) cases. Only 1 case had mild malnourishment (PNI 45-49), 5 had moderate malnourishment (PNI 40-44) and 19 had severe malnourishment (PNI <40).
RT-PCR Viral load was Low load (CT value >30) in 56 (70.0%), moderate (CT value 25-30) in 4 (5%) and High load (CT value <25) in 20 (25%) cases.
All the patients with Moderate and High viral load were admitted in ICU, only 14.3% of low load required ICU admission. Very high CRP levels (>50 mg/L) were observed in higher proportion of Severe Malnourished patients as compared to Moderate malnourished & Normal PNI (89.5% vs. 66.7% & 56.4%). Mortality was observed in higher proportion of Moderately & Severely Malnourished patients as compared to Normal PNI patients (75.0% & 44.0% vs. 20.4%).

Conclusion: We could not find any significant association between PNI severity and Systemic effects and comorbidities while diabetes was found to be a risk of mortality.

Keywords: COVID-19, PNI.

INTRODUCTION

Reports of new coronavirus disease originating from bats in early 2019 as the cause of a cluster of pneumonia cases in wuhan, a city in the Hubei province of china, initially the virus was named as "novel coronavirus 2019" but International committee of Coronavirus Study Group (CSG) renamed it "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2). Keeping in view the rampaging nature of COVID-19 WHO in January 2020 declared it as International health emergency and later on in March, 2020 as a pandemic.[4,5]

Cough, fever, short breath are initial symptoms of COVID-19 and in later stages it causes damage to vital organs. A wide range of clinical manifestations have been observed among COVID-19 patients, including asymptomatic disease to severe pneumonia having life threatening complications, ARDS (acute respiratory distress syndrome), dysfunction in multiple organs and mortality. These complications are major obstacles in appropriate care of COVID-19 patients.[12,13,14] COVID-19 patients seeking critical care place a huge burden on health care facilities.[15]

The prognostic nutritional index (PNI)16 is an objective assessment index reflecting the immune–nutritional status of patients. PNI can be easily calculated on the basis of routinely evaluated laboratory parameters (serum albumin and TLC) which are easy to repeat. PNI = [(10 × serum albumin (g/dL)) + (0.005 × total lymphocyte count/μl)].[17,18] PNI nutritional status was divided into 4 grades based on PNI value: normal (PNI ≥50), mild malnutrition (PNI 45–50), moderate to severe malnutrition (PNI 40–45), serious malnutrition (PNI <40)19,20. Prognostic nutrition index (PNI) has been found to be an independent prognostic indicator of various malignant tumor.[18,21,22] Poor nutritional status and immune dysfunction (especially depletion of T lymphocytes) have been considered to be risk factors for severe infection by SARS-CoV-2.[23]

Gong et al. (2020),[24] and Zhang et al. (2020),[25] had observed lower serum albumin and TLC levels were associated with COVID-19 severity, improvement and in hospital mortality. Wang et al. (2020),[26] opined that low level of albumin in non-survivors might attribute to intubation induced inadequate intake, reduced synthesis caused by liver dysfunction and increased consumption due to organ damage. They also suggested that decline in lymphocyte counts might be considered as a reflection of impaired immune function and sharply increasing cytokines. Albumin level and lymphocyte count which are the components of PNI, reflect nutritional and inflammatory status more comprehensively in COVID-19 patients.

Aim of the Study: To Study of correlation between Prognostic nutritional index (PNI) and short term clinical outcome in hospitalized covid -19 patients.

MATERIALS AND METHODS

The study was carried out at Department of Medicine, Era's Lucknow Medical College & Hospital (ELMCH). Government of Uttar Pradesh declared ELMCH during the first and second wave of COVID-19 infection for twenty-four months.All consecutive patients with Age >18 years and RT-PCR diagnosed cases of COVID-19 pneumonia attending the Era's Lucknow Medical College & Hospital were taken into study.

Prognostic nutritional index (PNI) was calculated on Day 1 of admission using formula: PNI =[(10 × serum albumin (g/dL)) + (0.005 × total lymphocyte count/μl)].[17,18] PNI was recalculated on Day 14 if patient stayed for period longer than 14 days.

PNI nutritional status was divided into 4 grades based on PNI value: normal (PNI ≥50), mild malnutrition (PNI 45–50), moderate to severe malnutrition (PNI 40–45), serious malnutrition (PNI <40).[19,20]

RT-PCR CT Load,[76]

The Ct values of PCR refer to amount of cycles required for the fluorescent signal to exceed background levels. In case of more target DNA, amplification is fast and fewer cycles are required (low Ct value) while for low amount of target DNA more cycles before the fluorescence (higher Ct value). Contact tracers also utilizes Ct values to prioritize their attention to patients with the highest viral genomic load, which indicates a high risk for transmissibility.

Severity of COVID-19 was assessed on CT involvement score as reported by Malpani et al. (2020),[77] on the basis of model proposed by Chung et al. (2020)78. Degree of air space opacification (GGO/consolidation) was assessed for five lung lobes. Scoring was done as:

Score 2 – 5–25% involvement.
Score 3 – 26–49% involvement.
Score 4 – 50–75% involvement.
Score 5 – >75% involvement.

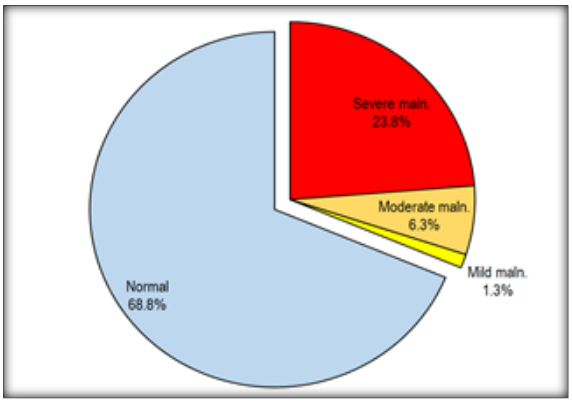
The total CT-IS was the sum of the individual lobar scores ranging from 0 (no involvement) to 25 (maximum involvement, when all the five lobes showed more than 75% involvement). The overall lung scores out of 25 was classified as mild, moderate, and severe, depending on the score range. The score between 0 and 9 was taken as a mild disease, 10–17 was taken as moderate disease, and the score range of 18–25 was taken as severe disease. Patients were followed up for 28 days from discharge.

Severity of COVID-19 was established using ICMR criteria,[75] as under

Mild	Patients with upper respiratory tract infection, may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache	Without evidence of breathlessness or hypoxia (normal saturation)
Moderate	Pneumonia with no signs of severe disease	With presence of clinical features of dyspnea and or hypoxia, fever, cough, including SpO2<94% (range 90-94%) on room air, Respiratory rate more or equal to 24 per minute.
Severe	Severe pneumonia	With clinical signs of pneumonia plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress, SpO2<90% on room air.

Ct value	Indication	Interpretation
< 25	High levels of SARS- CoV-2 genomic load	Patients with higher SARS-CoV-2 genomic loads are more likely to develop severe outcomes and require intubation and severe outcomes. Patient needs to be monitored.
25-30	Moderate levels of SARS-CoV-2 genomic load	Patients with higher SARS-CoV-2 genomic loads are more likely to develop severe outcomes and require intubation and severe outcomes. Patient needs to be monitored.
>30	Low levels of SARS- CoV-2 genomic load	Low SARS-CoV-2 genomic load can be found early in infection when replication has just begun. Additionally, it can indicate the later phases of infection after the virus has been cleared and has left behind remnants of its genomic content. Interpretation requires clinical context.

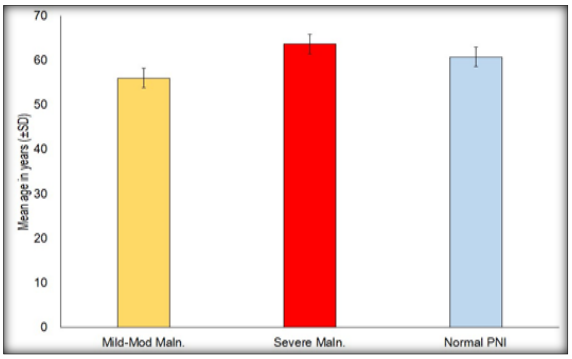
RESULTS



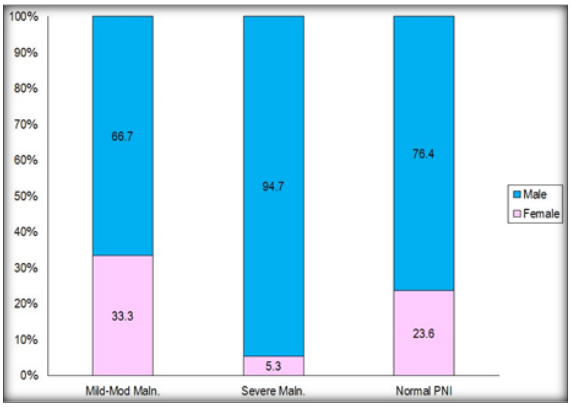
Graph 1: Nutritional Status (Based on PNI) of Study Population

Out of 80 patients PNI score was >50 in majority of cases (68.8%) who were considered as normal. Malnourishment was observed in 25 (31.3%) cases. Only 1 case had mild malnourishment (PNI 45-49), 5 had moderate malnourishment (PNI 40-44) and 19 had severe malnourishment (PNI <40).

RT-PCR Viral load was Low load (CT value >30) in 56 (70.0%), moderate (CT value 25-30) in 4 (5%) and High load (CT value <25) in 20 (25%) cases.



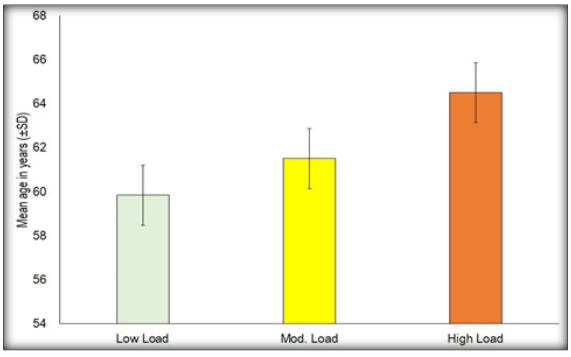
Graph 2.1: Association of PNI Severity with Age



Graph 2.2: Association of PNI Severity with Gender

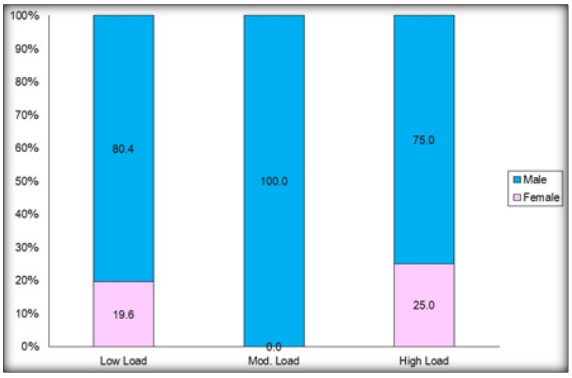
PNI was not found to be associated with demographic factors (Age & Gender) of COVID-19 patients.

Patients on distributing patients on the basis of viral load, 56 (70%) patients had Low viral load, 4 (5%) had Moderate viral load and 25% had High viral load. Following table shows association of Viral load with demographic profile of COVID-19 patients.



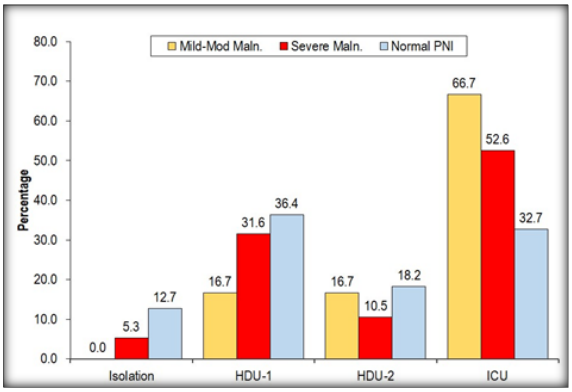
Graph 3.1: Association of Viral Load with Age

Though patients with Moderate and High viral load were older (61.50±8.89 & 64.50±11.66 years) as compared to those with Low viral load (59.84±16.95 years) but this difference was not found to be significant statistically.



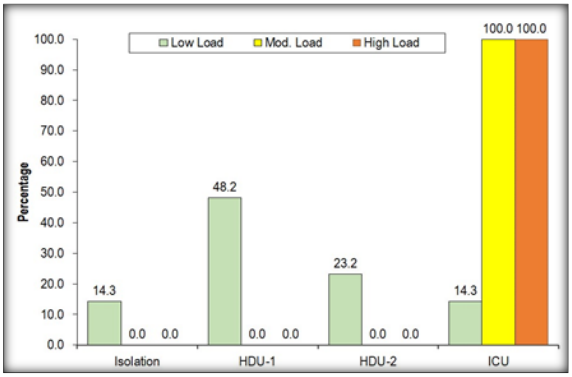
Graph 3.2: Association of Viral Load with Gender

Majority of patients enrolled in the study were male (n=64; 80%), in all the three groups with different viral load dominance of males was observed (80.4%, 100% & 75.0%). Difference in gender of patients with different viral load was not found to be significant statistically.



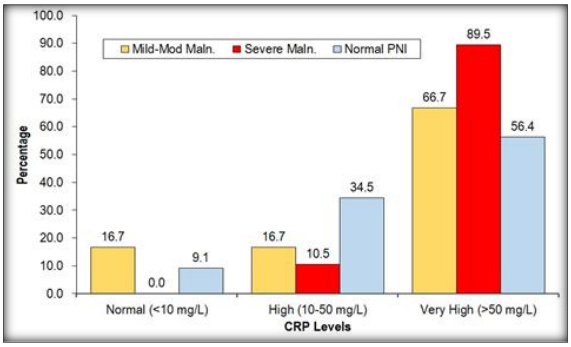
Graph 4: Association of PNI Severity with Hospital accommodation

Association of PNI with place of admission was not found to be significant statistically.



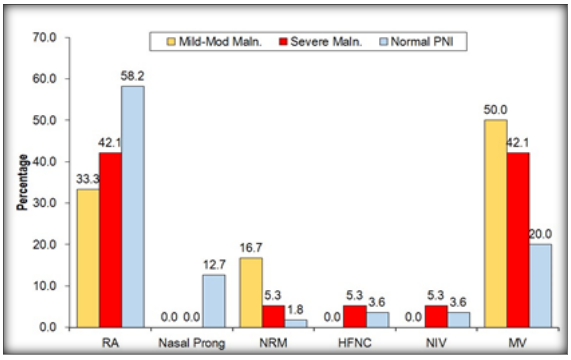
Graph 4.1: Association of Viral Load with Hospital Accommodation

All the patients with Moderate and High viral load were admitted in ICU, only 14.3% of low load required ICU admission, this difference was significant statistically.



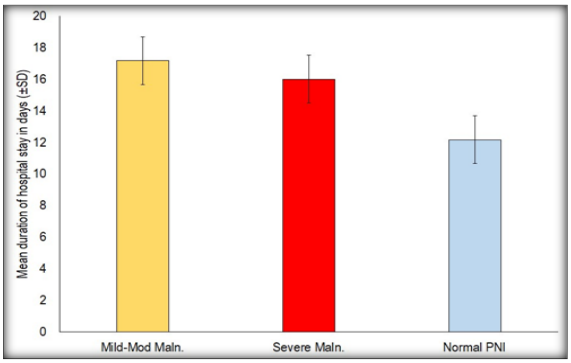
Graph 5: Association of PNI Severity with CRP levels

Very high CRP levels (>50 mg/L) were observed in higher proportion of Severe Malnourished patients as compared to Moderate malnourished & Normal PNI (89.5% vs. 66.7% & 56.4%) but this difference was not found to be significant statistically.



Graph 6: Association of PNI Severity and Oxygen Support

Higher proportion of non-malnourished (58.2%) as compared to Mild Moderate malnourished (33.3%) and Severe malnourished (42.1%) were on room air, rest required oxygen support. Mechanical ventilation was required in higher proportion of malnourished (Mild-Mod: 50%, Severe: 42.1%) as compared to non-malnourished (20.0%). Association of type of oxygen support and PNI was not found to be significant.



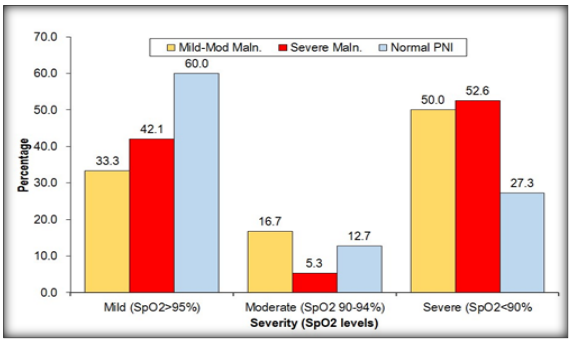
Graph 7: Association of PNI Severity and Duration of Hospital Stay

Duration of oxygen support was higher among Mild-moderately malnourished as compared to Severe and Normal PNI (10.25±6.85 vs. 8.27±2.15 vs. 6.50±3.04

days). Severe malnourished patients expired early therefore Oxygen support duration was lower.

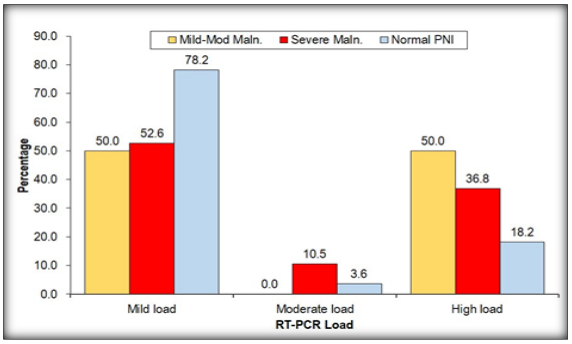
Duration of hospital stay was significantly higher among Moderately Malnourished & Severe malnourished as compared to Normal PNI covid-19 patients (17.17±10.98 & 16.00±4.54 vs. 12.16±5.63 days).

Day 1 Respiratory rate and Blood Urea of Malnourished cases (Mild Moderate + Severe) was significantly higher than those with Normal PNI. Day 1 lymphocyte levels of Malnourished cases was significantly lower as compared to those with Normal PNI. [Table 8]



Graph 8: Association of PNI Severity with SpO2 levels

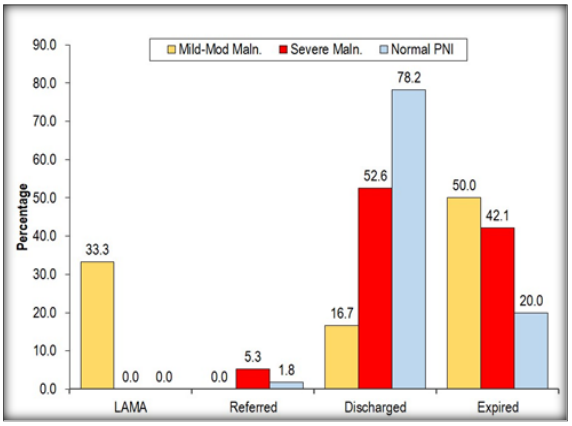
Out of 80 patients, at admission SpO2 levels of 43 (53.8%) was >95, were assessed as having Mild severity, 9 (11.3%) had SpO2 levels 90-94% were classified as having Moderate severity and rest 28 (35.0%) had oxygen levels <90% were classified as severe. In cases with mild abnormality of SpO2, proportion of cases with Normal PNI was higher as compared to Mild to Moderate. Malnourished and Severe Malnourished (60.0% vs. 33.3% & 42.1% while in cases with Severe abnormality of SpO2 proportion of cases with Mild to Moderate malnourished and Severe malnourished was higher as compared to Normal PNI (50.0% & 52.6% vs. 27.3%), but this difference was not found to be significant statistically.



Graph 9: Association of PNI Severity with Viral Load

Proportion of cases with Normal PNI was higher as compared to Mild to Moderate malnourished and Severe malnourished having Mild viral load (78.2% vs. 50.0% & 52.6%). Proportion of cases with Mild-Moderate malnourished and Severe Malnourished was higher as compared to Normal PNI having High viral load (50.0% & 36.8% vs. 18.2%). Association of Viral load and PNI was not found to be significant statistically.

Out of 80 patients, 24 (30.0%) patients were subjected to CT scan, 3 (12.5%) were adjudged as Moderate and 21 (87.5%) as Severe based on CT score (0-9 mild; 10-17 Moderate and 18-25 severe).

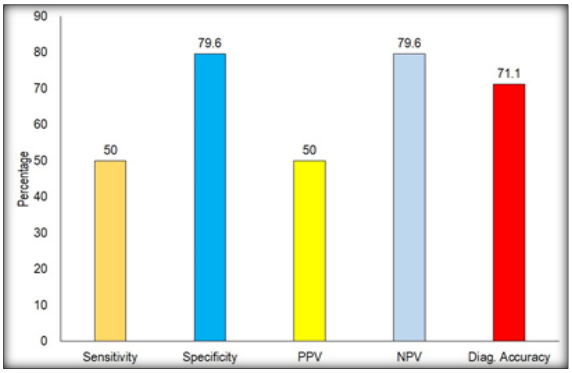


Graph 10: Association of PNI Severity with Outcome

Expiry was higher among Moderate & Severe malnourished (50.0% & 42.1%) as compared to Normal nutrition.

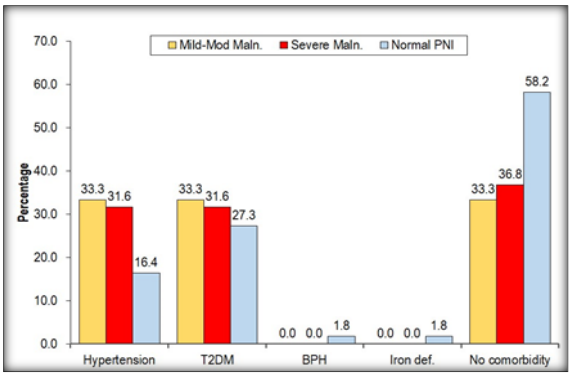
Graph 11: Association of PNI Severity with Final Outcome

Mortality was observed in higher proportion of Moderately & Severely Malnourished patients as compared to Normal PNI patients (75.0% & 44.0% vs. 20.4%) this difference was significant statistically.



Graph 11: Prognostic Value of Malnutrition for Prediction of Mortality

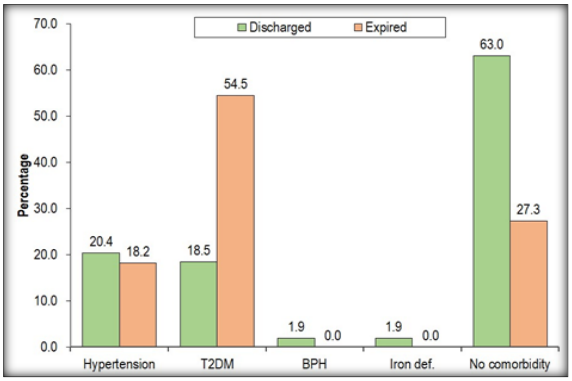
Despite significant difference in mortality rates of Malnourished and Normal PNI COVID-19 cases, assessment of malnourishment on the basis of PNI could predict the outcome accurately to the tune of 71.1% only. Sensitivity of above model was only 50.0% which equates to a flip coin model only.



Graph 12: Association of PNI Severity with Comorbidities

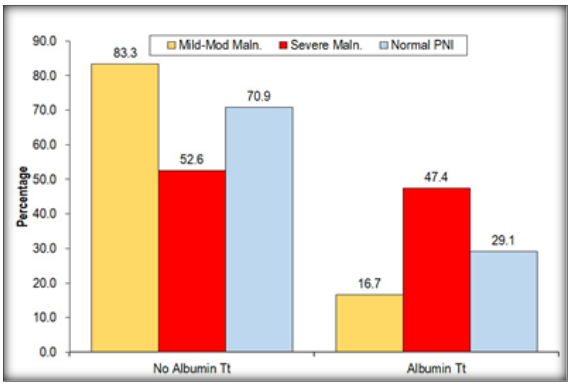
Above findings show that Moderate and Severe malnourished had higher exposure to Hypertension and diabetes as compared to normal PNI (33.3% & 31.6% vs. 16.4%) and (33.3% & 31.6% vs 27.3%), but this difference was not found to be significant.

Higher proportion of normal PNI cases had no comorbidity as compared to Moderate & Severe PNI (58.2% vs. 33.3% & 36.8%), this difference too was not found to be significant statistically.



Graph 13: Association of Comorbidities with Final Outcome

Risk of mortality was significantly higher in patients with T2DM.Survival among cases with no comorbidity was significantly higher as compared to mortality (63.0% vs. 2.3%)



Graph 14: Association of PNI Severity with Requirement of Albumin Treatment/Supplementation

Out of 80 patients enrolled in the study 26 (32.5%) required albumin treatment. Though higher proportion of severely malnourished patients as compared to mild to moderately malnourished and Normal PNI required albumin treatment (47.4% vs. 16.7% & 29.1%) yet this difference was not found to be significant statistically. Albumin treatment was given to patients with very low albumin levels, some patients with Normal nutrition having borderline Normal PNI to improve nutritional status.

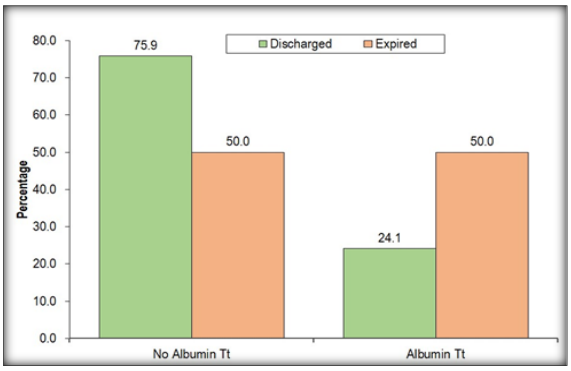


Figure 15: ?

Proportion of Expired cases was higher who received albumin treatment (50.0% vs. 24.1%) while proportion of discharged cases was higher who did not require No albumin treatment (75.9% vs. 50.0%). This difference was found to be significant statistically.

Patient Follow up: 28 days

Out of 54 discharged cases, 50 patients were telephonically followed till 28 days after their discharge, 4 patients who could not be followed up due to non-response at the contact details provided by them. During the follow up, no post-COVID complication such as change in smell or taste, depression, chest pain, palpitation etc. were reported by any of the patients.

Table 1: Distribution of Covid-19 patients according to Day 1 Prognostic Nutritional Index (PNI) (N=80)

SN		PNI Score	No. of cases	Percentage
1-	Malnourished (Cases)19,20		25	31.3
	Severe	<40	19	23.8
	Moderate	40-44	5	6.3
	Mild	45-49	1	1.3
2-	Normal	>50	55	68.8

Table 2: Association of PNI,[19,20] with Demographic Profile of Covid-19 patients (N=80)

S N	Demographic factors	Total (n=80)	Mild-Severe Moderate Malnourished Malnourished (n=6) (n=19)				Normal PNI (n=55)	
1-	Mean age ±SD (Range)	61.09±15. 49 (18- 88)	56.00±9.70 (44-70)		63.63±16.02(1888)		60.76±15.85 (29-88)	
	ANOVA		F= 0.586; p=0.559					
2-	Gender		No.	%	No.	%	No.	%
	Female	16	2	33.3	1	5.3	13	23.6
	Male	64	4	66.7	18	94.7	42	76.4
	Chi-square test		χ^2=1.455; p=0.228					

Table 3: Association of Viral load with Demographic Profile of Covid-19 patients (N=80)

SN	Demographic factors	Total (n=80)	Low load (n=56)		Mod. Load High load (n=4) (n=20)			
1-	Mean age±SD (Range)	61.09±15.49 (18-88)	59.84±16.95 (18-88)		61.50±8.89 (50-71)		64.50±11.66 (41-86)	
	ANOVA				F= 0.663; p=0.518			
2-	Gender		No.	%	No.	%	No.	%
	Female	16	11	19.6	0	0.0	5	25.0
	Male	64	45	80.4	4	100.0	15	75.0
	Chi-square test				χ^2=1.317; p=0.518			

Table 4: Association of PNI with Ward where Covid-19 patients admitted (N=80)

SN	Place of admission	Total (N=80)	Mild-Moderate Malnourished (n=6)		Severe Malnourished (n=19)		Normal PNI (n=55)	
			No.	%	No.	%	No.	%
1-	Isolation	8	0	0.0	1	5.3	7	12.7
2-	HDU-1	27	1	16.7	6	31.6	20	36.4
3-	HDU-2	13	1	16.7	2	10.5	10	18.2
4-	ICU	32	4	66.7	10	52.6	18	32.7
	Chi-square test		χ^2=5.154; p=0.524					

Table 4.1: Association of PNI with Ward where Covid-19 patients admitted (N=80)

SN	Place of admission	Total (N=80)	Malnourished (n=25)		Normal PNI (n=55)	
			No.	%	No.	%
1-	Wards (including Isolation ward)	48	11	44.0	37	67.3
2-	ICU	32	14	56.0	18	32.7

χ^2=3.879; p=0.049

Table 4.2: Association of Viral load with Ward where Covid-19 patient admitted (N=80)

SN	Place of admission	Total (N=80)	Low load (n=56)		Mod. Load (n=4)		High load (n=20)	
			No.	%	No.	%	No.	%
1-	Isolation	8	8	14.3	0	0.0	0	0.0
2-	HDU-1	27	27	48.2	0	0.0	0	0.0
3-	HDU-2	13	13	23.2	0	0.0	0	0.0
4-	ICU	32	8	14.3	4	100.0	20	100.0
	Chi-square test		χ^2=51.429; p<0.001					

Table 5: Association of PNI with CRP Levels of Covid-19 patients (N=80)

SN	CRP levels (mg/L)	Total (N=80)	Mild-Moderate Malnourished (n=6)		Severe Malnourished (n=19)		Normal PNI (n=55)	
			No.	%	No.	%	No.	%
1-	Normal (<10 mg/L)	6	1	16.7	0	0.0	5	9.1
2-	High (10-50 mg/L)	22	1	16.7	2	10.5	19	34.5
3-	Very High (>50 mg/L)	52	4	66.7	17	89.5	31	56.4
	Chi-square test65.0				χ^2=7.907; p=0.095			

Table 6: Association of Level of malnourishment with Oxygen Support Covid-19 patients admitted (N=80)

SN	Oxygen Support	Total (N=80)	Mild-Severe Moderate Malnourished Malnourished (n=19) (n=6)				Normal PNI (n=55)	
			No.	%	No.	%	No.	%
1-	RA	42	2	33.3	8	42.1	32	58.2
2-	Nasal Prong	7	0	0.0	0	0.0	7	12.7
3-	NRM	3	1	16.7	1	5.3	1	1.8
4-	HFNC	3	0	0.0	1	5.3	2	3.6
5-	NIV	3	0	0.0	1	5.3	2	3.6
6-	MV	22	3	50.0	8	42.1	11	20.0
	Chi-square test		χ^2=12.053; p=0.282					

Table 7: Association of PNI with Duration of Oxygen Support and Hospital Stay

SN	Duration	Mild-Moderate Malnourished			Severe Malnourished			Normal PNI			ANOVA	
		n	Mn	SD	n	Mn	SD	n	Mn	SD	F	'p'
1-	Oxygen support	4	10.25	6.85	11	8.27	2.15	24	6.50	3.04	2.721	0.079
2-	Hospital stay	6	17.17	10.98	19	16.00	4.53	55	12.16	5.63	4.263	0.018

Table 8: Association of PNI with Hemodynamic and Biochemical Parameters

SN	Parameters	Malnourished (n=25)		Normal PNI (n=55)		Student 't' test	
		Mean	SD	Mean	SD	't'	'p'
1-	SBP	117.44	16.79	116.55	15.80	0.230	0.819
2-	DBP	67.28	13.97	67.31	10.98	-0.010	0.992
3-	HR	90.68	20.56	86.29	16.63	1.015	0.313
4-	RR	28.36	8.94	23.47	7.94	2.454	0.016
5-	SpO2	89.48	7.58	92.33	7.57	-1.558	0.123
6-	Blood Urea mg/dl	75.70	79.29	42.53	29.83	2.722	0.008
7-	Creatinine mg/dl	1.69	1.36	1.51	1.58	0.488	0.627
8-	Albumin	2.90	0.36	3.02	0.43	-1.188	0.238
9-	Lymphocyte	5.24	2.30	17.91	7.65	-8.096	<0.001

Table 9: Association of PNI with Severity of disease (according to ICMR)

SN	Severity	Total (N=80)	Mild-Moderate Malnourished (n=6)		Severe Malnourished (n=19)		Normal PNI (n=55)	
			No.	%	No.	%	No.	%
1-	Mild (SpO_2>95%)	43	2	33.3	8	42.1	33	60.0
2-	Moderate (SpO_2 90- 94%)	9	1	16.7	1	5.3	7	12.7
3-	Severe (SpO_2<90%	28	3	50.0	10	52.6	15	27.3
	Chi-square test		χ^2=5.224; p=0.265					

Table 10: Association of PNI with Severity of disease (RTPCR load) (N=80)

SN	Viral Load	Total	Mild-Moderate Malnourished (n=6)		Severe Malnourished (n=19)		Normal PNI (n=55)	
			No.	%	No.	%	No.	%
1-	Mild load	56	3	50.0	10	52.6	43	78.2
2-	Moderate load	4	0	0.0	2	10.5	2	3.6
3-	High load	20	3	50.0	7	36.8	10	18.2
	Chi-square test				χ^2=6.941; p=0.139			

Table 11: Association of PNI with Outcome of Covid-19 patients admitted (N=80)

SN	Outcome	Total (N=80)	Mild-Moderate Malnourished (n=6)		Severe. Normal PNI (n=19)		(n=55)	
			No.	%	No.	%	No.	%
1-	LAMA	2	2	33.3	0	0.0	0	0.0
2-	Referred	2	0	0.0	1	5.3	1	1.8
3-	Discharged	54	1	16.7	10	52.6	43	78.2
4-	Expired	22	3	50.0	8	42.1	11	20.0
	Chi-square test		χ^2=33.051; p<0.001					

Table 12: Association of PNI with Final Outcome of Covid-19 patients admitted (N=76)

SN	Outcome	Total (N=76)	Moderate Malnourished (n=4)		Severe Malnourished (n=18)		Normal PNI (n=54)	
			No.	%	No.	%	No.	%
1-	Discharged	54	1	25.0	10	55.6	43	78.2
2-	Expired	22	3	75.0	8	44.4	11	20.0
	Chi-square test		χ		^{2}=8.158; p=0.017			

Table 13: Prognostic Value of Malnutrition (PNI based) to Predict Mortality

	Expired SN PNI Status (n=22)			Discharged (n=54)
1-	Malnourished (Moderate-Severe)		11	11
2-	Normal PNI		11	43
True Positive	False Positive	False Negative		True Negative
11	11	11		43

Sensitivity	Specificity	PPV	NPV	Accuracy
50.0	79.6	50.0	79.6	71.1

Table 13: Association of PNI with Comorbidities (N=80)

SN	Outcome	Total (N=80)	Mild-Moderate Malnourished (n=6)		Severe Malnourished (n=19)		Normal PNI (n=55)		Statistical significance	
			No.	%	No.	%	No.	%	χ^2	'p'
1-	Hypertension	17	2	33.3	6	31.6	9	16.4	2.520	0.284
2-	T2DM	23	2	33.3	6	31.6	15	27.3	0.194	0.907
3-	BPH	1	0	0.0	0	0.0	1	1.8	0.460	0.794
4-	Iron def.	1	0	0.0	0	0.0	1	1.8	0.460	0.794
5-	No comorbidity	41	2	33.3	7	36.8	32	58.2	3.407	0.182

Table 14: Association of Comorbidities with outcome (N=76)

SN	Outcome	Total (N=76)	Discharged (n=54)		Expired (n=22)		Statistical significance	
			No.	%	No.	%	χ2	'p'
1-	Hypertension	17	11	20.4	4	18.2	0.047	0.828
2-	T2DM	22	10	18.5	12	54.5	9.864	0.002
3-	BPH	1	1	1.9	0	0.0	0.413	0.521
4-	Iron def.	1	1	1.9	0	0.0	0.413	0.521
5-	No comorbidity	40	34	63.0	6	27.3	7.987	0.005

Table 15: Association of PNI and Albumin Treatment Requirement (N=80)

SN	Albumin treatment	Total (N=80)	Mild-Moderate Malnourished (n=6)		Severe Malnourished (n=19)		Normal PNI (n=55)	
			No.	%	No.	%	No.	%
1-	No Albumin Tt	54	5	83.3	10	52.6	39	70.9
2-	Albumin Tt	26	1	16.7	9	47.4	16	29.1

χ^2=2.892; p=0.236

Table 16: Albumin Treatment with outcome (N=76)

SN	Outcome	Total (N=76)	Discharged (n=54)		Expired (n=22)	
			No.	%	No.	%
1-	No Albumin Tt	52	41	75.9	11	50.0
2-	Albumin Tt	24	13	24.1	11	50.0

χ2=4.863; p=0.027

Table 18: Demographic Characteristics with outcome (N=76)

SN	Demographic Characteristics	Discharged (n=54)	Expired (n=22)	Statistical significance
1-	Mean age ±SD	59.59±17.00	65.00±9.92	't'=–1.571; p=0.120
2-	M(%):F(%)	44 (81.5%): 10(18.5%)	18 (81.8%: 4(18.2%)	□^{2}=0.001; p=0.973

DISCUSSION

On the eve of compilation of the present work the most satisfactory thing in the life of a health care personnel is that number of new cases of this deadly disease (COVID-19) which had been declared as a pandemic by World Health Organization are negligible. The journey of present work started with the surroundings of scared faces with uncertainty on effectiveness of treatment, hope of success of vaccination and irradiation of the deadly disease. Longer duty hours in highly infected surroundings, with inconvenience of wearing of PPE kits, quarantine period away from familial atmosphere were frustrating but were once in a life-time experience for healthcare professionals. With an urge to provide relief to the ailing community by adoption of advanced practices in patient care & monitoring was the mission of the present study.

Data provided by Ministry of Health & Family welfare of Government of India COVID-19 spread in 19% of the elderly people but 63% of reported deaths of COVID-19 account for patients ≥60 years of age 79,80. Therefore, old age was identified as a risk of mortality among COVID-19 but quest to identify the older patients who could survive in COVID-19 and COVID-19 like

conditions gained our attention towards prognostic nutritional status which is a laboratory investigation (albumin and TLC) based indicator of immunity and nutritional status. Though BMI is a well-known indicator of nutritional status and do not require any intervention but in COVID-19 like situation it has limited practical applicability when correct physical measurements could not be assessed and PNI has an advantage of indicating immune status of immunocompromised patients like COVID.

The present study was conducted to ascertain whether the age-old practice of predicting the clinical outcome on the basis of chronological age of the patient should continue or advanced practices on the basis of clinical condition, immunity and nutritional status should be adopted to predict clinical outcome, one of the advanced practices was assessment of prognostic nutritional index, which is a laboratory based and reliable. We are of the opinion that once we can visualize the outcome, we can change the outcome with change in management strategies.

With an objective of assessment of prognostic nutritional index (PNI) in hospitalized COVID-19 patients and to correlate the PNI with clinical outcome. The present study included 80 diagnosed cases of COVID-19 pneumonia. Mild, moderate and severe cases were included in the present study. If present study could provide any useful findings to be applied in clinical practice that should be dedicated to the patients included in the study.

BMI is most commonly used to assess nutritional status, involves no cost and it can be calculated even without help of any instrument in no time. BMI of patients admitted to hospital in chronic conditions cannot be calculated, nutritional assessment of these patients is done by alternative tools. PNI is an alternate to BMI for nutritional assessment which is based on routinely evaluated laboratory parameters serum albumin and TLC. for assessment PNI has been used to assess the nutritional condition of patients in different chronic diseases and surgical interventions (Gastric carcinoma, Lung cancer, heart failure, cardiac surgery) for assessment of prognosis and mortality.[47,48,49,50,51,52,53,54,55,56,57.58,59]

In the present study we adopted the four grades of PNI as ≥50 – Normal, 45-50 Mild malnutrition, 40-45 moderate to severe malnutrition and <40 serious malnutrition as adopted by Kanda et al,[19] and Liu et al.[20]

The present study was a cross sectional observational study to assess the nutritional status of COVID-19 using prognostic nutritional status (PNI) and to study its role on outcome. Observational studies are advantageous as they provide descriptive data and information of particular disease without interfering with the treatment protocol without any financial burden on patient/researcher.

Research design of majority of the reported literature on role of PNI in COVID-19 patients had been done using the observational research design, only a few studies have used retrospective data.[65,67,74] Retrospective studies also do not interfere with the standard treatment approach and interventions but availability of structured data is sometimes difficult. The study design adopted in the present study is in concordance with majority of the studies executed with similar research problem.

In the present study 80 consecutive patients with mild, Moderate and severe COVID-19 infection had been included, however sample size in other reported studies vary from as low as 101 to 1605. Low sample size in previous retrospective studies had been observed in studies by Hu et al.(n=122)65, Wei et al. (n=295),[67] and Tuncei (n=146)74. Only cross-sectional study with very close sample size was by Wang et al. (n=101).[66] However, sample size employed in other cross-sectional design is much higher than that in the present study: 200500 patients had been included by Wang et al. (n=450)61; Cinaret al. (n=294)63; Ekiniet al. (n=282)64; Fernandes et al. (n=309),[70] >500 patients had been included in studies by Bayram et al. (n=748), Arsian & Bas (n=1579),[69] Mathiodakis et al. (n=1605).[71]

The present study had been conducted after projecting sample size using statistical tools to which we adhered. The proposed sample size for the present study was much smaller than most of the previous studies employing a crosssectional design. With a larger sample size, we could have explored and concluded the findings with greater confidence. Though sample size of the present study remains a limitation yet can be justified because it has been calculated scientifically.

COVID-19 Severity

In the present study only 80 COVID-19 patients were included. In majority of studies reviewed in the

present study, severity of COVID-19 patients has either not been mentioned or only proportion of severe patients only had been mentioned.

In the present study COVID-19 patients aged 18-88 years had been included, mean age of patients was 61.09±15.49 years, majority of patients were male (80%). On comparing the average age of patients enrolled in contemporary studies, it was observed patients in the present study were older. Wang et al,[61] enrolled patients aged 39-79 years with female dominance

(54.2%). Average age of patients was nearly 55 years in studies reported by Cinar et al,[63] and Ekiniet al,[64] Wang et al,[66] and Fernandes et al.[70] Average age of patients in the study reported by Hu et al,[65] was very low (44.0 ±13.4 years) but age of patients included in their study was wider (10-82 years). However, average age of patients included in Wei et al,[67] (Median: 60 years) and Tuncel et al,[74] (Mean: 62 years) was quite close to that in present study.

Only Wang et al,[61] Cinaret al,[63] and Wang et al,[66] had conducted their studies where female dominance (54.2%, 53.4%, 53.5% respectively) had been reported. In rest of the literature reviewed though male dominance of patients had been reported but present study comprised of 80% of males, while in other studies the male population comprised of 52-60%. Lower representation of females in the present study can be justified on the fact that in India males are more exposed to risk factors due to greater participation in livelihood, personal habits (smoking, alcohol) and preference in treatment by family members.[81,82]

Prevalence of Malnutrition

In the present study we found that out of 80 patients, majority of patients (68.7%) had normal nutritional status (PNI ≥50). Only 25 (31.3%) had malnutrition: 1 (1.3%) had mild malnutrition (PNI: 45-50), 5 (6.3%) had moderate (PNI 40-45) level of malnutrition, 23.8% had severe (PNI <40) malnutrition.

Findings of Fernandes et al,[70] is very close to the present study, they reported 71.5% of COVID-19 patients had normal nutrition (PNI <40) as compared to 68.7% reported in the present study.

Cinaret al. (2021),[63] instead of using already defined severity of nutritional status by PNI divided the PNI values of 294 patients in tertiles to find its association with mortality, 98 (33.3%) patients each were in T1 (PNI <43.7%), T2 (PNI 43.7-51.4) and T3 (PNI >51.4), values of T3 tertile are very close to the normal category of the present study. These values also indicate that approximately 60-65% patients were malnourished, which as compared to the findings of present study is quite higher.

Contrasting results had also been reported by Aktan et al,[68] and Yenibertiz et al,[72] who used different cut-off of PNI severity where PNI ≤35 is considered as Severe, 35-38 as Moderate and >38 as Normal; while in the present study normal nutrition is considered as >50 PNI. Equating the data approximately 50-65% patients fall under malnourished category.

On overviewing the findings of other studies wherein instead of categorizing patients into different severity levels of malnutrition, quantitative values have been used for observing association of PNI and outcome.

As discussed above, small sample size in the present study might be the reason for low prevalence of malnourished COVID-19 patients.

Age and Gender

In the present study significant association of PNI with Age and gender has not been observed. While Cinar et al,[63] had found older age and Male gender to be significantly associated with lower PNI. Similarly, Yenibertiz et al,[72] also found significantly higher proportion older (>65 years) and male patients in severe malnourished category. Ekinci et al,[64] also reported significant but inverse correlation between age & PNI indicating that with increase in age PNI declines. Association of malnourishment with older age and male gender has been accepted in various studies on non-COVID

Patients.[48,49,51,55]

Similar to our study Arslan & Bas,[69] did not find any significant association of gender and malnutrition. Various reports on non-COVID patients also supported the findings of present study wherein no significant association of PNI with age and gender has been reported (Tanemura et al., Wang et al.).[57,58]

ICU Requirement

In the present study we observed that all the patients with moderate-high viral load required ICU admission. Allocation of hospital accommodation and Severity of malnutrition did not show significant association. Significantly higher proportion of malnourished patients (Mild-moderate and severe) required ICU admission as compared to Normal PNI patients.

The findings of present study are logical in nature wherein patients with higher viral load required ICU admission, and lower nutritional compromised (Mild-Moderate and Severe malnourished) had significantly higher requirement of ICU. Our findings are supported by Bayram et al,[62] and AlShami et al.[73] In other studies ICU admissions either are not mentioned or are associated with other outcomes.

In the present study we did not find any significant association of PNI Severity with CRP levels and type of oxygen support. Significantly higher CRP levels among severe COVID-19 infected patients had been reported by Hu et al,[66] but they had not correlated CRP levels and PNI. CRP is an inflammatory marker ofCOVID-1983 and patients with higher CRP levels had lower daily caloric intakes, lower serum mean albumin levels,[84] which is an essential component for PNI assessment therefore significant association of CRP and PNI severity is expected. but absence of this relationship could be blamed to small sample size of the present study.

Hospital stay in the present study was significantly associated with PNI Severity. Malnourished patients had significantly higher hospital stay. In different

non-COVID studies longer hospital/ICU stay of patients with low PNI
had been reported.[46,49,54,55] Larger hospital stay is indicative of lower immunity, Severity of PNI (lower PNI) is directly correlated with albumin levels and TLC, of these low TLC has been attributed to disease progression in HIV and chronic diseases.[85]

In the present study we have also observed that malnourished patients had higher Respiratory rate and blood urea and lower levels of lymphocyte counts. PNI based nutritional status indicate lower PNI levels (<50) as compromised nutritional status. Higher respiratory rate is indicative of low oxygen levels in the body and higher blood urea indicative of higher stress on kidneys which might be due to low water/nutrient intake. These conditions at least represent the aggravated respiratory condition and kidney functions which have a cause-effect relationship with malnutrition. As already discussed above, lymphocyte count is a component to calculate PNI and is directly correlated with PNI, low TLC contributes for lower PNI. In the present study mortality rate was 28.9%. Among malnourished cases 50.0% mortality and among normal PNI cases 20.0% mortality had been reported. A wide variation in mortality rates had been reported in different studies. Lower mortality rates as compared to the present study had been reported by various authors as: Bayram et al,[62] found a lower mortality rate 6.3% in a study with larger sample size (n=748) and had also associated with low PNI scores. Similarly, Wang et al. reported a mortality rate of 5.9% only in a study with equitable sample size of the present study (n=101). Cinar et al),[63] had reported mortality rate of approximately 10% (30 out of 294) and lower mortality scores for higher PNI. Wang et al.61 reported a 17.3% mortality rate in a female dominant population showing significant association with low PNI scores.

Relatively similar to the present study mortality rates had been reported by Wei et al. (26.7%),[67] in a retrospective study and did not find any significant association with PNI.

Ekinci et al,[64] proposed a cut off at <41.2 to predict mortality with 78.7% sensitivity and 84.2% specificity.

Reasons of variation in mortality rates lie in regional differences of study locations, healthcare facilities, COVID-19 spread, study design and demographic factors which had already been discussed.

In the present study albumin treatment was required to 26 (32.5%) patients, final outcome of 24 patients who required albumin treatment was known,11 (45.8%) of those expired after albumin supplementation/treatment this confirms albumin (an essential component of PNI) as a prognostic marker of mortality.

We could not establish any significant association between PNI Severity and comorbidities and have found diabetes to be significantly associated with higher mortality rates. Despite the limitations of the present study the fact cannot be ignored that it is a pioneer work in this field in North India.

The findings of the present study indicate that prognostic nutritional Index (PNI) which is being applied for prediction of clinical outcome of patients with chronic diseases and surgeries can be used to predict the clinical outcome in situations like COVID-19 too, without ignoring the role of comorbidities, age, gender, social status on the outcome. Further studies with larger sample size to overcome the limitations of the present study are recommended.

CONCLUSION

Chief findings of the present study were as under

1. Majority patients 55 (68.8%) were assessed which had normal PNI, only 1 (1.3%) had mild malnutrition, 5 (6.3%) had moderate malnutrition and 19 (23.8%) had severe malnutrition. Only 31.2% COVID-19 patients included in the present study were malnourished. Further comparisons were made among severe, mild-moderate malnourished and normal PNI patients.
2. PNI severity and viral load did not show significant association with age and gender of patients.
3. Malnourished patients were at significantly higher risk of ICU admissions.
4. Higher CRP levels and Oxygen requirement did not show significant association with PNI severity. Hospital stay of malnourished patients was significantly higher.
5. Malnourished patients had significantly higher levels of Respiratory rate, Blood urea and lower levels of Lymphocyte.
6. In the present study, we could not find any significant association between PNI severity and Systemic effects and comorbidities while diabetes was found to be a risk of mortality.
7. Mortality rates of malnourished patients were significantly higher. Differentiation of malnourished i.e. PNI <50 and Normal PNI i.e. ≥50, could predict mortality with diagnostic accuracy of 71.1%, with low sensitivity levels (50.0%) and average specificity (79.6%).
8. Mortality of Covid-19 patients did not show any significant association with Age and gender.
9. Albumin treatment has insignificant impact over the mortality /survival but the number of patients is too small to make a conclusion.

ConclusioThe above findings indicate that though PNI severity was associated with mortality but accuracy to predict mortality was not encouraging, especially sensitivity levels were only 50.0% which equates to flip coin model. The findings of the present study might not be as encouraging as expected due to small sample size but can be recognized as an initial

step to associate prognostic nutritional index and clinical outcome in COVID-19 like situation.

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