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Original Research Paper

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HBA1C, AN OUTCOME PREDICTOR FOR PATIENTS ADMITTED IN COVID ICU TREATED WITH HAEMODIALYSIS FOR ACUTE KIDNEY INJURY

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ABSTRACT

Context: COVID-19, initially identified as a respiratory illness, was soon found to cause manifestations of almost every organ system in patients of different profiles. Thus, there is a need to understand possible predictors in various patient settings to improve the outcome. **Aims:** To study HbA1c as an outcome predictor for patients admitted in COVID ICU with acute kidney injury undergoing haemodialysis as a treatment modality. **Methods and Material:** From July 2020 to January 2022, data of COVID patients who underwent haemodialysis for acute kidney injury were collected. Baseline parameters and outcomes were recorded and comparison between diabetics and non-diabetics of similar COVID severity were compared. Survival analysis as per HbA1c was also performed. **Results:** Total 126 patients were included in this study out of which 25, 21 and 26 non-diabetics had mild, moderate and severe disease respectively, classified as per Computed Tomography Severity Index. 14, 16 and 24 diabetics had mild, moderate and severe disease respectively. The number of survivors in each severity class was significantly higher in non-diabetics as compared to diabetics. Furthermore, in diabetics, the survival curve was significantly better in patients with an HbA1c of 6.5-9% as compared to those with an HbA1c of >9%. **Conclusions:** This study reveals that intervening COVID ICU patients with haemodialysis for AKI can significantly reduce the mortality provided they have a better pre-infection glycemic control as predicted by HbA1c levels. Also, there is a need to lower the dialysis-initiation threshold in COVID positive patients with AKI.

KEYWORDS : HbA1c, predictor, COVID ICU, haemodialysis, AKI

INTRODUCTION

Diabetes mellitus, most common endocrine disorder of 21st century, tipped the scales against survival in our fight with COVID, deadliest pandemic humanity has ever seen. Hyperglycemia during hospitalisation was associated with poor outcome in COVID[1] attributing it to cytokine release consequently increasing insulin resistance[2].

Acute renal dysfunction worsens this atrocious amalgam of diabetes and COVID both contributing to the renal insult which acts on ACE2 receptor[3] of proximal tubules and podocytes and the latter causes microvascular injury.

Our goal is to study these factors acting in concert using HbA1c for stratification and how haemodialysis can benefit this multi-system plight.

SUBJECTS AND METHODS

Institutional ethics committee–human research approved the study. Study procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

The present study includes patients admitted in COVID ICU, undergoing haemodialysis for acute kidney injury at haemodialysis unit at a tertiary care centre from July 2020 to January 2022.

This was a retrospective observational study. Hospital data of all the COVID-19 patients in ICU, undergoing haemodialysis for acute kidney injury at haemodialysis unit at a tertiary care centre were recorded for their history, presenting complaints, baseline biochemical parameters, and their trends during the hospital stay and their changes with haemodialysis and outcomes associated. Patients with chronic kidney disease on maintenance haemodialysis and those with a haemoglobin of <10g/dl were excluded. All the patients were tested COVID positive by RT-PCR. Haemodialysis were performed in these patients for any of the emergency indications of acute kidney injury (refractory acidosis, refractory hyperkalaemia, anuria, uraemia, refractory fluid overload). Decision to undertake multiple haemodialysis sessions were made as per the treating physician's discretion and the patient's needs.

The presentation of the categorical variables was done in the form of number and percentage (%). The quantitative data were presented as the mean±SD. The comparison of the variables across groups which were quantitative in nature were analysed using unpaired t test. The data entry was done in Microsoft Excel spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 21.0. For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS

126 patients admitted in COVID ICU intervened with haemodialysis at a tertiary care centre were included in this retrospective study. They were categorised as per the Computed Tomography Severity Index (CTSI) into three groups, i.e., mild (score <8), moderate (8-16) and severe (17-25)[4]. Each group was further divided into diabetics (HbA1c >=6.5%) and non-diabetics (HbA1c<6.5%).

As shown in Table 1, demographic comparison on the basis of age, gender and BMI was done. On comparison within the subgroups, non-diabetics and diabetics had uniform age-distribution (p value of difference of 0.24, 0.198 and 0.288 for mild, moderate and severe CTSI respectively) although mean age was higher in the group with severe CTSI (54.58±16.37 and 58.79±10.47 years for non-diabetics and diabetics respectively) than moderate (45.57±17.33 and 52.31±12.63 years for non-diabetics and diabetics respectively) or mild (40.17±11.94 and 44.79±11.30 years for non-diabetics and diabetics respectively) CTSI. Heterogeneity in sex distribution among diabetics and non diabetics was only statistically significant in the mild CTSI group [19 (76.00%) in non-diabetics vs 6 (42.86%) in diabetics, p=0.038]. The diabetics of moderate and severe CTSI groups had significantly higher BMI as compared to non-diabetics [21.01±4.46 in non-diabetics vs 23.91±3.86 in diabetics, p=0.045 for moderate CTSI and 20.73±2.78 in non-diabetics vs 23.72±3.98 in diabetics, p=0.002 for severe CTSI]. This difference was also

seen in the mild CTSI group (20.63±3.23 in non-diabetics vs 22.36±3.66 in diabetics) although not significant (p=0.135).

Table 1: Comparison of characteristics of COVID positive non-diabetics and diabetics

		Mild CTSI			Moderate CTSI			Severe CTSI		
		Non-diabetics (n=25)	Diabetics (n=14)	P value	Non-diabetics (n=21)	Diabetics (n=16)	P value	Non-diabetics (n=26)	Diabetics (n=24)	P value
Demographics										
	Age (years)	40.176± 11.94	44.79± 11.30	0.24	45.57± 17.33	52.31± 12.63	0.198	54.58± 16.37	58.79± 10.47	0.288
	Males	19 (76.00%)	6 (42.86%)	0.038	15 (71.42%)	12 (75.00%)	0.809	17 (65.38%)	19 (79.17%)	0.278
	BMI (kg/m2)	20.63± 3.23	22.36± 3.66	0.135	21.01± 4.46	23.91± 3.86	0.045	20.73± 2.78	23.72± 3.98	0.002
Haematological parameters										
	Hemoglobin (g/dl)	11.79± 2.17	10.44± 0.72	0.036	12.76± 2.75	11.31± 2.28	0.096	10.88± 2.48	10.63± 2.59	0.729
	NLR	5.85± 3.03	6.31± 3.54	0.685	10.82± 3.78	11.92± 5.37	0.469	14.35± 5.89	16.86± 6.72	0.167
	Platelet count (lac/mm3)	1.93± 0.42	1.84± 0.46	0.523	1.60± 0.50	1.46± 0.50	0.405	1.28± 0.52	1.32± 0.62	0.790
	D-dimer (mg/l)	1.48± 1.46	2.38± 3.57	0.273	4.59± 2.48	5.75± 3.04	0.209	7.32± 2.42	6.93± 2.40	0.390
Kidney function tests										
	Blood Urea (mg/dl)	139.20± 36.50	178.40± 71.95	0.074	166.05± 52.43	217.21± 73.94	0.018	222.96± 60.30	271.42± 74.01	0.014
	Serum Creatinine (mg/dl)	7.22± 1.51	8.21± 3.49	0.327	7.39± 3.91	10.31± 4.24	0.037	9.49± 3.21	12.33± 4.39	0.013
No of HD done	1.72±0.54	1.44± 0.36	0. 092	1.43± 0.60	1.69±0.70	0.232	1.65± 0.69	2.17± 1.43	0.121	
Outcome	No. Of survivors	24 (96.00%)	12 (85.71%)	0.039	10 (47.62%)	4 (25.00%)	0.026	7 (26.92%)	1 (3.85%)	0.028

There was no significant difference between diabetics and non-diabetics when the haematological parameters NLR (p=0.685, 0.469 and 0.167 for mild, moderate and severer respectively), platelet count (p=0.523, 0.405 and 0.790 for mild, moderate and severer respectively) and D-Dimer (p=0.273, 0.209 and 0.390 for mild, moderate and severer respectively) were compared. Haemoglobin was lower in diabetics of mild, moderate and severe CTSI groups (p= 0.036, 0.096 and 0.729 respectively).

Overall diabetics had a greater renal injury than their non-diabetic counterparts, with significantly higher urea [166.05±52.43 in non-diabetics vs 217.21±73.94 in diabetics, p=0.018 for moderate CTSI and 222.96±60.30 in non-diabetics vs 271.42±74.01 in diabetics, p=0.014 for severe CTSI] and serum creatinine [7.39±3.91 in non-diabetics vs 10.31±4.24 in diabetics, p=0.037 for moderate CTSI and 9.49±3.21 in non-diabetics vs 12.33±4.39 in diabetics, p=0.013 for severe CTSI] in the moderate and severe CTSI groups. Even in the mild CTSI group, the blood urea and serum creatinine was higher in diabetics although this difference failed to meet statistical significance [139.20±36.50 in non-diabetics vs 178.40±71.95 in diabetics, p=0.074 for blood urea and 7.22±1.51 in non-diabetics vs 8.21±3.49 in diabetics, p=0.327 for serum creatinine].

More or less similar number of dialysis was done in the non-diabetics as compared to diabetics across mild [1.72±0.54 vs 1.44±0.36, p=0.092], moderate [1.43±0.60 vs 1.69±0.70, p=0.232] and severe [1.65±0.69 vs 2.17±1.43, p=0.121] CTSI groups.

The number of survivors was significantly higher in the non-diabetics irrespective of severity of CTSI as seen in Figure 1, [(96.00% vs 85.71%, p=0.039 for mild), (47.62% vs 25.00%, p=0.026 for moderate), (26.92% vs 3.85%, p=0.028 for severe)]. Amongst the diabetics, those with an inadequate pre-infection glycaemic control (HbA1c >9) had worse outcome when compared to diabetics with an HbA1c between 6.5 and 9 as shown by the Kaplan Meier survival curve in Figure 2.

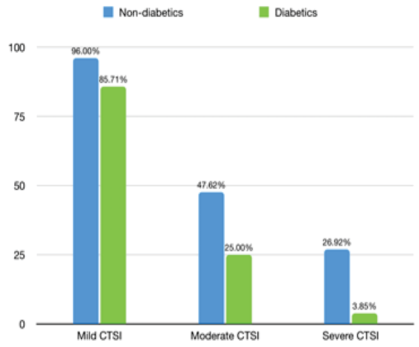

Figure 1: Comparison of survival of non-diabetics and diabetics across different disease severities

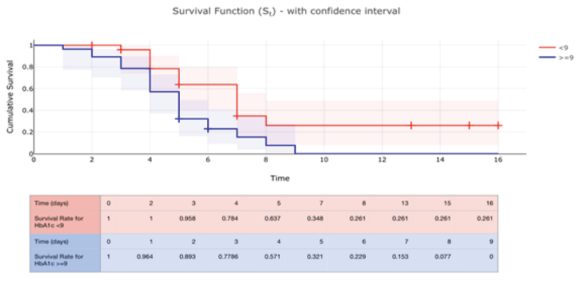

Figure 2: Kaplan Meier Survival curves of diabetics stratified as per glycemic control with a cut off HbA1c of 9%

DISCUSSION

In this retrospective study, among 126 patients admitted in COVID ICU (54 patients with diabetes and 72 without diabetes), patients with diabetes developed more severe AKI as compared to non-diabetics.

Stratification of patients into mild, moderate and severe CTSI groups was done to compare post-interventional survival and impact of haemodialysis between diabetics and non-diabetics across the entire spectrum of COVID severity.

The patients with severe lung involvement as per CTSI had a higher mean age than those with mild and moderate CTSI. This is in consistence with existing literature[5]. A similar age profile of diabetics and non-diabetics in our study negates the effect of age as a confounding factor among patients with similar degrees of lung involvement. Across the whole spectrum of COVID severity, majority of patients were males irrespective of diabetes status. This can also be attributed it to an overall higher hospitalisation in males as supported by previous studies on sex differences[6]. Higher BMI of diabetics in moderate and severe CTSI and not in mild CTSI suggests that patients with a lower BMI tend to have a milder disease even in diabetics.

Since COVID is a disease of systemic inflammatory state, CTSI alone cannot predict disease severity and outcome. Haematological parameters such as D-dimer (a measure of thromboembolic phenomena), platelet count (a measure of systemic inflammation) and NLR (a measure of sepsis)[7] are an important addendum to CTSI for anticipating clinical severity. In our patients, the diabetics and non-diabetics did not differ significantly in terms of these haematological parameters. Their equal distribution in our study helps us to affirm the homogeneity between diabetics and non-diabetics.

In the analysis of kidney function tests, higher serum urea and creatinine values in diabetics is indicative of more grievous renal insult. Diabetes has already been implicated to be associated with worse cardiopulmonary outcomes in COVID-19[8]. Our findings suggest that diabetics are also at a higher risk of renal dysfunction and consequent abysmal outcomes. Furthermore, diabetics and non-diabetics received a comparable number of haemodialysis sessions probably owing to the shorter hospital stay ending in early mortality amongst diabetics. Amongst diabetics, those with uncontrolled HbA1c (>9%) showed a steep fall in the survival curve compared to their counterparts with a better glycaemic control (HbA1c <9%). Using HbA1c as an indicator of glycaemic control is a better option over blood glucose levels at presentation because the latter has a high degree of variability owing to multitude of factors such as sepsis, stress response, over zealous use of steroids which was rampant during the pandemic.

The gist of our findings is that patients with similar profile in terms of age, sex, BMI, haematological parameters and COVID severity, differing only in their pre-infection glycaemic control tend to have significantly different outcomes.

Our study is unique as no study, to the best of our knowledge, has ventured in the direction of outcome assessment in those ICU patients with an unfavourable combination of COVID, diabetes and AKI intervened with haemodialysis.

CONCLUSION

Our tertiary care centre providing haemodialysis in perilous COVID times gave us an opportunity to intervene on patients with the worst possible outcomes. It is noteworthy that a good number of patients could be still saved from the precarious fate sprung upon them by the pandemic using haemodialysis as an interventional modality. There is a constant need to improve our knowledge on COVID among patients with various comorbidities to tackle any future unpredictable mutant strains with the strongest foot forward. Hence, all known cases of diabetes should be treated to a tight glycaemic control to give them a better chance in the fight for survival. Also, to reap maximum benefits of haemodialysis in diabetics with COVID, we perhaps need to lower the threshold for initiation of dialysis.

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