Original Article

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Clinical Course and Outcome of Eleven Maintenance Hemodialysis Patients with COVID-19 in Iraq

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ABSTRACT

Background and objectives: SARS-CoV-2 may affect the hemodialysis population as well as be possibly associated with their higher mortality rate. The objectives of the study were to describe the clinical presentations, assess laboratory markers, and risk factors for mortality.

Methods: This was an observational single-center retrospective study of two hemodialysis units in Basra from May 1, 2020 to June 1, 2020.

Results: Among the 11 patients, four (36.4%) died. Compared to the survivors, non-survivors had significantly longer dialysis vintage (16 ± 14.7 vs 9 ± 5.2; $P = 0.048$) and lower day 10 lymphocyte count (3.75 ± 0.96 vs 9.4 ± 5.6; $P = 0.036$). Age and laboratory parameters were not associated with the increased hazard risk for death.

Conclusions: The SARS-CoV-2 infection in hemodialysis units was linked with a high mortality rate.

Keywords: COVID-19, Hemodialysis, Dialysis Unit, Mortality Rate.

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) is an acute respiratory illness caused by the novel coronavirus SARS-CoV-2. Patients with comorbidities are more susceptible to the infection and, thus, more likely to experience severe illness with high mortality, especially patients with end-stage kidney disease on maintenance hemodialysis. They have a high risk of developing the severe disease compared to the general population as they are older, have less efficient immune responses, and are exposed to many infections during the dialysis procedures.[1] Clinical presentations in the general population range from the mild course in up to 80% of the cases to the severe course in up to 15% and the extremely serious course requiring ICU admission in up to 3–5%.[2-4] Diarrhea may dominate the clinical presentations by 80%, followed by fever and fatigue in 60%.[5] The symptoms and laboratory markers in patients on maintenance hemodialysis with COVID-19 compared to those without COVID-19 were relatively mild initially with low levels of inflammatory cytokines.[6] The reported cases from two dialysis centers in Lombardy, Italy were 18 out of 60 and four out of 170 patients on maintenance hemodialysis.[7] The mortality rate was reported to be 28% based on a cohort study from Spain with 25 patients on chronic dialysis and 40% developed ARDS.[8]

The objectives of this observational retrospective study were to describe the clinical manifestations of the SARS-CoV-2 infection in the hemodialysis unit, assess the laboratory markers of severity, and risk factors for mortality.

MATERIALS AND METHODS

Data source, study designs, and participants

This was an observational retrospective single-center study examining patients on the maintenance hemodialysis program with positive real-time RT-PCR testing for SARS-CoV-2 from May 1, 2020 to June 1, 2020. The data sources were drawn from medical records; additionally, the details of the demographic, clinical features, laboratory parameters, treatment lines, and mortality rate were registered. The study gained the approval of the Ethical Committee of the University of Basra and the Ministry of Health (Iraq).

Measurements

The dialysis vintage was measured in months and the time to death from admission in days. The laboratory test and unit of measurements included hemoglobin (g/dl), lymphocyte count (%), serum C-reactive protein (mg/dl), serum ferritin (ng/ml), serum lactate dehydrogenase (U/l), and serum albumin (mg/dl).

Covariates

The demographics consisted of age, gender, and body mass index while the history reported encompassed the social history for smoking, medical history of chronic diseases, symptoms of COVID-19, type of vascular access, and duration of hemodialysis. Moreover, examination for signs of volume overload were conducted. The laboratory investigations were executed at admission

and on day 10 after hospitalization, with the treatment lines documented.

Treatment lines

The doses of the drugs were administered as the following: hydroxychloroquine (400 mg bid at day one, then 200 mg bid for four days comprising a total of five days), azithromycin (500 mg od for five days), unfractionated heparin (5000 IU every six hours IV), and dexamethasone (8 mg every 12 hours IV for five days).

Statistical analysis

The qualitative variables were presented as frequency and percentage whereas the quantitative variables as mean (SD) for continuous normal distribution and median (interquartile range) for continuous skewed distribution. The comparative analysis for qualitative variables between two different groups (survivors vs non-survivors) was conducted using the chi-square test or Fisher's exact test. The comparative analysis for quantitative variables between the two groups was performed using an independent sample t-test. Further, the cox proportion was employed to assess the hazard ratio for in-hospital mortality. All statistical analyses were performed with the SPSS version 25; the statistical significance was considered a two-sided P value < 0.05.

RESULTS

Out of 850, 11 patients on the maintenance hemodialysis program followed in two reference hemodialysis units were hospitalized with confirmed COVID-19 starting on May 1, 2020. The baseline demographic and clinical characteristics are shown in Table 1. The mean age was 54 ± 7 years and 72% were male. All patients had hypertension (100%), with other comorbidities being less frequent: diabetes (27%), coronary artery disease (27%), and heart failure (36%). The most common symptoms at admission were dyspnea (100%), fever and cough (82%), followed by nausea, vomiting, and diarrhea (36%). The mean duration for hemodialysis was 12 ± 10 months, 36% were dialyzed via the arteriovenous fistula, 64% dialyzed via a central venous catheter, and 46% had volume overload during the hospitalization period.

There were n differences in demographics and clinical characteristics between survivors and non-survivors, with the exception of non-survivors having had longer dialysis vintage (9 ± 5.2 vs 16 ± 14.7; P = 0.048).

The laboratory characteristics are presented in Table 2. After 10 days of admission, there was falling hemoglobin, percentage lymphocyte count, albumin, and increasing serum ferritin, lactate dehydrogenase, and C-reactive protein. There were no differences in the baseline and day 10 parameters between survivors and non-survivors, except for the day 10 lymphocyte count (9.4 ± 5.6 vs 3.75 ± 0.96; P = 0.036).

The treatment characteristics are illustrated in Table 3. Most patients received heparin (63.6%), steroids (63.3%), azithromycin and hydroxychloroquine (54.5%), and convalescent plasma (9%); with no differences between the two groups.

The hazard ratio for in-hospital mortality is displayed in Table 4; neither age nor laboratory parameters were hazard risks for in-hospital mortality.

The comparison of baseline and day 10 laboratory parameters between survivors and non-survivors are depicted in Fig. 1. At day 10 of their admission, the non-survivors had the lowest lymphocyte count and albumin and the highest serum C-reactive protein, ferritin, and lactate dehydrogenase levels compared to the survivors.

The non-survivors had more volume overload than the survivors as shown in Fig. 2. Additionally, they had longer dialysis vintage than the survivors (Fig. 3).

The median time to death was 8.5 days and all deaths were resulted from respiratory failure.

The use of hydroxychloroquine and azithromycin were more frequent in less severe cases while heparin and steroid were used more frequently in severe cases as shown (Fig. 4).

Table 1. Baseline demographics and clinical characteristics

Variables	Total (n = 11)	Survivors (n = 7)	Non-survivors (n = 4)	*P value*
Age, year	53.8 ± 7.3	51.9 ± 5.8	57.3 ± 9.2	0.256
Male	8 (72.2)	6 (85.7)	2 (50)	0.491
Body mass index	26.6 ± 2.6	25.9 ± 2.8	28 ± 1.8	0.207
Smoking	7 (63.6)	4 (57.1)	3 (75)	1.000
Comorbidity				
Hypertension	11 (100)	7 (100)	4 (100)	
Diabetes	3 (27.3)	2 (28.6)	1 (25)	1.000
Coronary artery disease	3 (27.3)	1 (14.3)	2 (50)	0.491
Heart failure	4 (36.4)	2 (28.6)	2 (50)	0.576
Chronic obstructive pulmonary disease	1 (9.1)	1 (14.3)	0 (0)	1.000
Asthma	1 (9.1)	1 (14.3)	0 (0)	1.000
Symptoms				
Fever	9 (81.8)	6 (85.7)	3 (75)	1.000
Cough	9 (81.8)	6 (85.7)	3 (75)	1.000
Dyspnea	11 (100%)	7 (100)	4 (100)	
Diarrhea, nausea, or vomiting	4 (36.4)	2 (28.6)	2 (50)	0.576
Volume overload	5 (45.5)	2 (28.6)	3 (75)	0.242
Vascular access				
Central venous catheter	7 (63.6)	6 (85.7)	1 (25)	0.088
Arteriovenous fistula	4 (36.4)	1 (14.3)	3 (75)	0.088
Duration on hemodialysis, months	11.5 ± 9.7	9 ± 5.2	16 ± 14.7	0.048

Data is n (%), mean ± SD.

Table 2. Laboratory characteristics at admission and after 10 days after the clinical onset

Laboratory variables	Total	Survivors	Non-survivors	*P value*
Hemoglobin, g/dl				
Baseline	9 ± 1.3	9.1 ± 1.4	9 ± 1.3	0.917
Day 10	8.5 ± 1.1	8.6 ± 1.3	8.4 ± 0.8	0.781
Lymphocyte count, %				
Baseline	12.5 ± 5.1	12.6 ± 6.2	12.5 ± 3	0.980
Day 10	7.4 ± 5.2	9.4 ± 5.6	3.75 ± 0.96	0.036
Serum C-reactive protein, mg/dl				
Baseline	66.9 ± 48.7	59.3 ± 56	80.3 ± 35.4	0.467
Day 10	98 ± 62.7	90.4 ± 67.7	111.5 ± 59.6	0.608
Serum ferritin, ng/ml				
Baseline	376.3 ± 158.7	339.1 ± 167.1	441.3 ± 138.6	0.310

Day 10	555 ± 209.7	479.3 ± 218.9	687.5 ± 118.1	0.071
Serum lactate dehydrogenase, U/l				
Baseline	254.5 ± 59.4	242.9 ± 41	275 ± 86.6	0.417
Day 10	399.8 ± 126.2	365.7 ± 135.9	459.5 ± 93.3	0.212
Serum albumin, g/dl				
Baseline	3.45 ± 0.3	3.5 ± 0.3	3.3 ± 0.2	0.180
Day 10	3 ± 0.5	3.2 ± 0.6	2.95 ± 0.1	0.346

Data are mean ± SD.

Table 3. Treatment characteristics in survivors and non-survivors

Treatment variables	Total (n = 11)	Survivors (n = 7)	Non-survivors (n = 4)	*P value*
Azithromycin	6 (54.5)	4 (57.1)	2 (50)	1.000
Hydroxychloroquine	6 (54.5)	4 (57.1)	2 (50)	1.000
Heparin	7 (63.6)	3 (42.9)	4 (100)	0.194
Steroids	7 (63.3)	3 (42.9)	4 (100)	0.194
Convalescent plasma	1 (9.1)	1 (14.3)	0 (0)	1.000

Data are n (%).

Table 4. Hazard ratio of age and 10 day laboratory variables for in-hospital mortality

Variables	Adjusted HR	*P value*	95% CI
Age	6.68	0.293	0.19, 230
Lymphocyte count	0.026	0.282	0.0, 20
Serum C-reactive protein	1.3	0.290	0.79, 2.2
Serum ferritin	1	0.769	0.96, 1
Serum lactate dehydrogenase	0.85	0.323	0.62, 1.2
Serum albumin	0.0	0.377	0.0, 8.2

HR, hazard ration; CI, confidence interval.

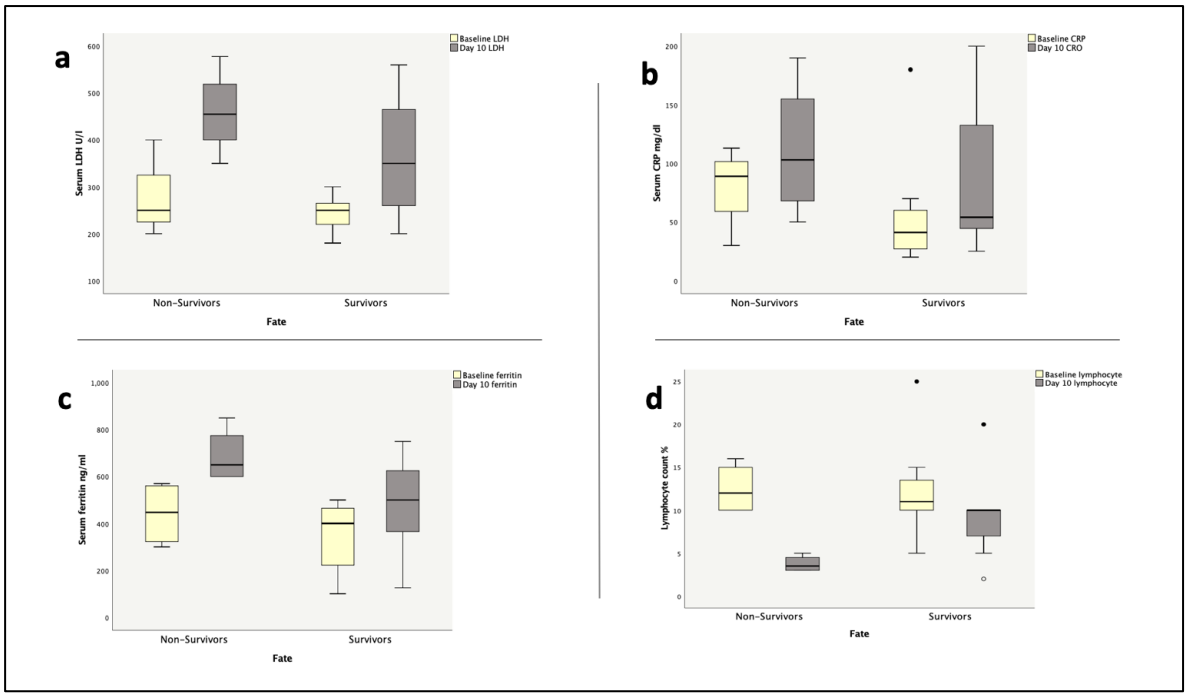

Figure 1. Association of laboratory markers with patients' fate: A) serum lactate dehydrogenase; B) serum C-reactive protein; C) serum ferritin; and D) lymphocyte count.

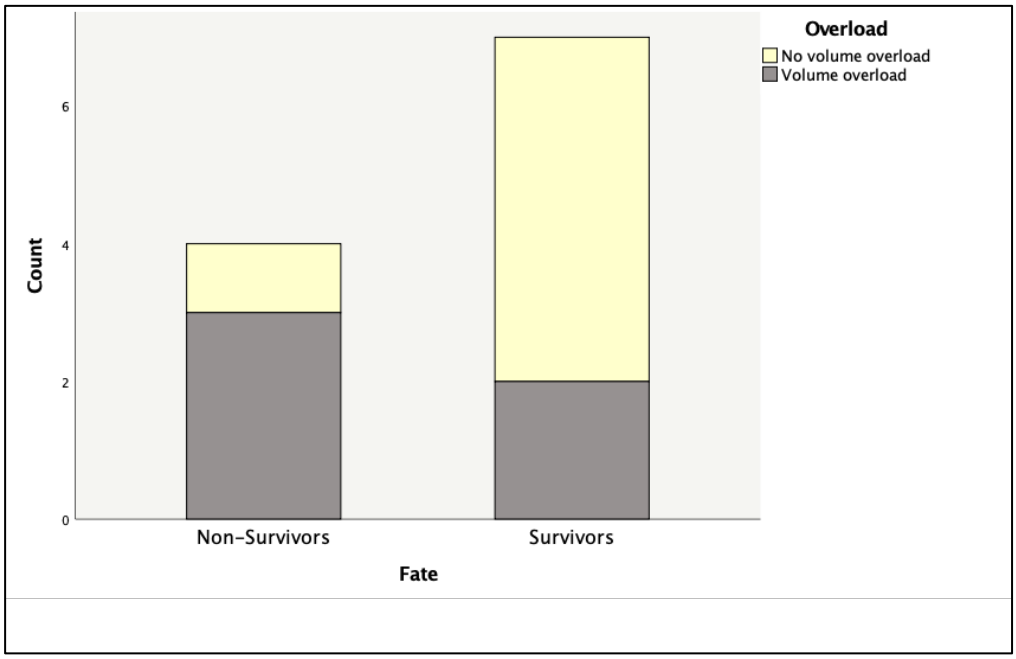

Figure 2. Proportions of volume overload by patients' fate status

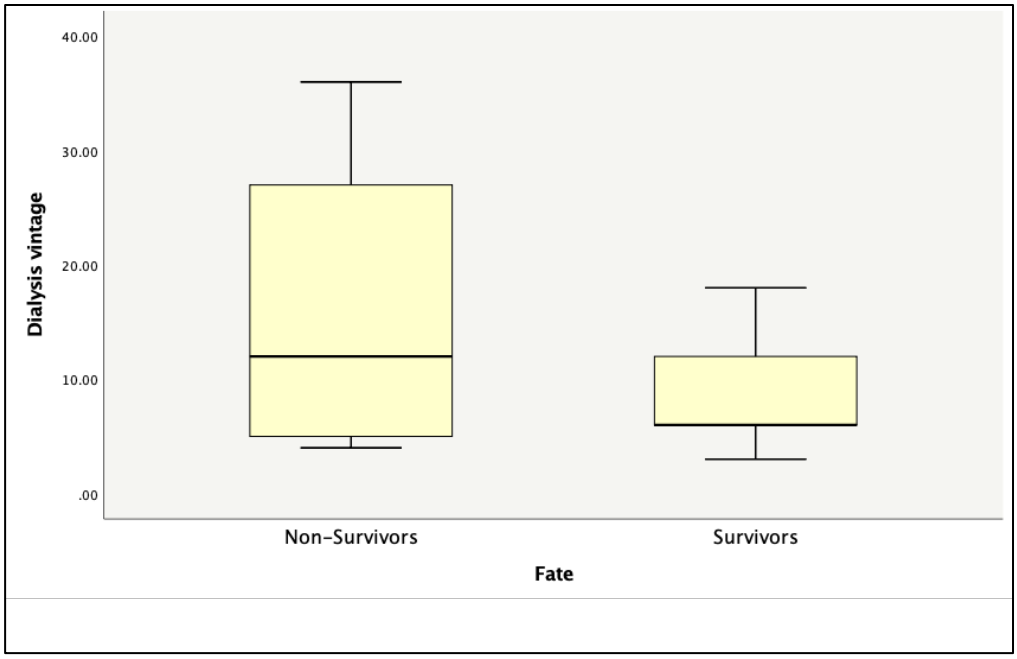

Figure 3. Dialysis vintage per survivors vs non-survivors

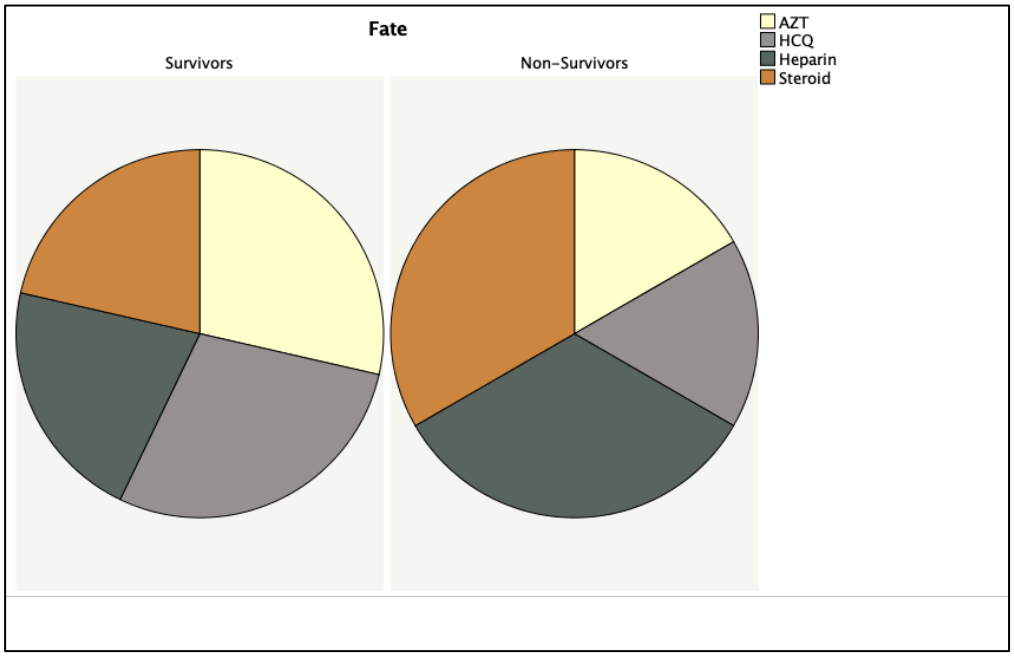

Figure 4. Proportions of medications used per patients' fate status

DISCUSSIONS

The main aim of the present study was to describe the clinical features, laboratory parameters, treatment lines, and mortality of patients on maintenance hemodialysis who were hospitalized with COVID-19 at two

hemodialysis units. Yiqiong et al. compared the blood test results in 37 maintenance hemodialysis patients with those from unaffected maintenance hemodialysis patients and healthy subjects. They also reported on mortality (6 of them died, 31 were hospitalized).[6] The clinical presentations of the study cohort were similar to the general population regarding fever (82% vs 88%) but had a higher rate of cough (82% vs 58%).[9] Diarrhea was less frequent in the present study (36.4% vs 80%) but the fever was more frequent (82% vs 60%).[10]

To date, as there is no effective therapy in the maintenance hemodialysis patients, we utilized the same treatment protocols used in the general population. Hydroxychloroquine and azithromycin were administered to approximately half of the patients. Gautretet et al. reported a virological cure with this combination in a select cohort of patients, but there is very low certainty of the efficacy results with this treatment, mainly due to a very high-risk selection bias, making any claims of effectiveness highly uncertain.[11] Hydroxychloroquine was not associated with a lower or higher risk for the composite endpoints.[12] The use of corticosteroids for the treatment of moderate to severe COVID-19 with lung injury was reported by many studies, some presented positive while others negative outcomes.[13–15]

Corticosteroids were revealed to reduce the need for mechanical ventilation and, hence, reduce mortality.[15,16] Dexamethasone use was associated with decreased mortality in hospitalized patients.[17] Heparin use may lower mortality because of the high risk of thrombogenesis with COVID-19 infection 18. In the present study, steroid and heparin were used more frequently in severe cases but, unfortunately, the patients died due to severe respiratory failure.

The mortality rate in the present study (36.4%) was much higher than that observed in the general population (1.4%–8%).[2–4] It was higher than the 26% ICU mortality rate reported by Grasselli et al. in Italy.[2] This variation may be explained by the presence of multiple comorbid conditions, especially the high cardiovascular comorbidity observed in patients with end-stage kidney disease. The mortality rate in our cohort was higher than that reported by Yiqiong et al. (36.4% vs 16.2%), although our patients were younger (54 vs 66 years); this may be due to the type of care provided for the patients. It was slightly higher than the study of 36 patients on maintenance hemodialysis from Spain (36.4% vs 30.5%), even though our patients were younger (54 vs 71 years).[19] The mortality rate reported in other series from Italy were higher and lower than the mortality rate of our study: Scarpioni et al. found a mortality rate of 41% in Piacenza (n = 41) and Alberici et al. a mortality rate of 25% in Brescia (n = 21).[20,21]

In the current study, the non-survivors had more volume overload, longer dialysis vintage, higher day 10 serum CRP, LDH, ferritin, and lower lymphocyte and albumin which was in agreement with a study from Spain.[19]

Our study has some limitations. First, being a retrospective study, some laboratory tests such as D-dimer, procalcitonin, and

interleukin-6 were not conducted. Second, we are not aware of the exact incidence of COVID-19 in our dialysis facility because we performed real-time RT-PCR only in symptomatic patients. Third, at the time of writing the draft of the study, some patients, were still hospitalized and some new cases may be discovered, potentially affecting our findings. Finally, a small sample size may affect the interpretations of the results.

CONCLUSIONS

In conclusion, the mortality rate among hospitalized patients on maintenance hemodialysis was high. Serial laboratory parameters were useful in assessing the risk of mortality.

Acknowledgment

We acknowledge the efforts of all the medical staff, patients, and laboratory personnel in the hemodialysis units.

Statement of Ethics

The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patients gave informed consent to their participation and the study protocol was approved by the University of Basra and Ministry of Health committee on human research.

Conflict of Interest Statement

The authors declared that they have no conflict of interest.

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Author Contributions

Data collection: Hayder Aledan, Mohammed Al Atbee, and Hassanein Alkhammas; Statistical analysis: Hayder Aledan; Writing the draft: Hayder Aledan; Revision and validation: Hayder Aledan, Mohammed Al Atbee, and Hassanein Alkhammas.

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