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ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) IN HAIL REGION, SAUDI ARABIA

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ABSTRACT: Background: Acute respiratory distress syndrome (ARDS) is a medical condition occurring in critically ill patients characterized by extensive inflammation in the lungs and associated with several complications. Therefore, the present study aimed to identify the common risk factors associated with ARDS in Hail Region, Northern Saudi Arabia. **Methodology:** This study investigated retrospectively 68 patients with ARDS clinical presentations during the period from January 2015 to January 2016 in King Khalid Hospital, Hail, Saudi Arabia. **Results:** Out of 68 patients with ARDS clinical presentations, ARDS was verified in 38/68 (55.9%). Out of 38 ARDS patients, 21/38(55.3%) were males and 17/38 (44.7%) of the 68 studied patients, pneumonia, trauma, H1N1 infection and fibrosis were identified in 50(73.5%), 3(4.4%), 13(19.1%) and 12 (17.6%), respectively. Out of the 38 ARDS patients, 29/38 (76.3%) died. **Conclusion:** ARDS is common in Hail Region and a common cause of patients to be admitted to specialized intensive care units. Inhalation injuries associated with pneumonia, H1N1 infection and fibrosis were an independent risk factor for ARDS. The mortality rate observed in the study patients was high and associated with ARDS diagnosis.

INTRODUCTION: Acute respiratory distress syndrome (ARDS) happens in 10% of all intensive care unit (ICU) patients, in 23% of all mechanically ventilated patients, with 5.5 cases per ICU bed each year. ARDS employs a considerable disease burden, with 40% of patients dying in the hospital. The latest progress in our understanding of the epidemiology of ARDS has created important visions into the incidence, risk factors, demographics, management and outcomes from this distressing clinical syndrome [1].

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Estimates of the prevalence of the ARDS in high- and middle-income countries fluctuate from 10.1 to 86.2 per 100,000 person-years in the general population [2]. About a third of patients getting mechanical ventilation in the ICU were at risk of ARDS. Pulmonary complications often arise in patients at risk of ARDS, and their clinical outcome is worse compared with those not at risk of ARDS [3].

In spite of substantial developments in our understanding and management of patients with ARDS, the morbidity and mortality from ARDS leftovers in elevation. Given the inadequate number of effective treatments for recognized ARDS, the strategic emphasis of ARDS inquiry has moved in the direction of ascertaining patients with or at high risk of ARDS early in the course of the causal disease, when plans to decrease the progress and

advancement of ARDS and related organ failures can be methodically assessed [4]. Human corona-viruses (HCoVs) were regarded as harmless respiratory pathogens in the past. However, after the outbreak of the severe acute respiratory syndrome (SARS) and the appearance of the Middle East respiratory syndrome (MERS), HCoVs were given global attention [5]. MERS is a highly fatal respiratory disease caused by a novel single-stranded, positive-sense RNA betacoronavirus (MERS-CoV).

Although most cases of MERS have happened in Saudi Arabia and the United Arab Emirates, cases have been reported in Europe, the USA, and Asia in people who traveled from the Middle East or their contacts [6]. Middle East respiratory syndrome coronavirus carries a high mortality rate in patients who require ICU admission, with a significant number of patients developing multiorgan system failure (MOSF) [7]. MERS coronavirus pneumonia with ARDS has high mortality in patients with comorbidities. The backbone of treatment is careful ARDS management [8]. Therefore, the present study aimed to identify the common risk factors associated with ARDS in Hail Region, Northern Saudi Arabia.

MATERIALS AND METHODS: This was a retrospective study conducted in King Khalid hospital involving 68 patients, who were previously admitted to ICU as having acute respiratory syndrome and were referred to the Pulmonary Medicine Department for Respiratory Complications, during the period from January 2015 to January 2016. All medical records of the patients were retrospectively revised with respect to their demographic characteristics, ARDS, laboratory data.

Diagnosis of respiratory complications was considered if clinical/pulmonary function tests were suggestive and High-Resolution CT Scan (HRCT) was consistent with a pulmonary condition (Pleural Edema, Pneumonia, and Pleural Effusion). The patient's identification data were retrieved from the medical records at the Pulmonary Medicine Department at King Khalid Hospital. Data were extracted to take information on age, gender and proved-diagnosis of ARDS. Patients without any identifiable cause for pulmonary complications were considered to have idiopathic pulmonary conditions and were excluded.

Data Analysis: Statistical analysis was done using SPSS version 23.0 (SPSS Inc., Chicago, IL, USA). Associations were presented as Odds Ratios (ORs) with their corresponding 95% confidence intervals (CIs). A value of $p<0.05$ was considered as statistical significance.

Ethical consent: The ethical committee approved the protocol of the present study at the College of Medicine, University of Hail.

The informed consent was agreed about by the Pulmonary Medicine Department at King Khalid Hospital. Ethical Approval Number: EC-00059.

RESULTS: In the present study, 68 patients with ARDS related symptoms aged 1 to 95 years, were investigated. The patients included 33(48.8%) males and 35(50.5%) males; their mean age was 48 years. Out of the 68 patients with ARDS-related complaints, 38(55.9%) were confirmed with ARDS, and the remaining 30(44.1%) were diagnosed with other respiratory conditions.

ARDS have commonly observed among males 21(55.3%) *vs.* 17(44.7%) females. The risk of ARDS among males and the 95% confidence interval and relative risk (RR) was: RR (95% CI) = 1.3102(0.8544 to 2.0090), P = 0.2155, as indicated in **Table 1** and **Fig 1**. Most of ARDS patients were older (60+ years = 14 (37%) and younger (<18years =13(34%).

The risk associated with older age; RR (95% CI) = 1.6163 (1.0240 to 2.5512), P = 0.0392. The risk associated with younger age; RR (95% CI) = 2.0057 (1.4537 to 2.7674), P < 0.0001, as indicated in **Table 1** and **Fig. 1**. Out of the 38 ARDS patients, 25(66%) presented with fever.

Fever was statistically significantly associated with ARDS; RR (95% CI) = 2.1930 (1.2123 to 3.9670), P = 0.0094. Cough indicated in 27(71%) of the ARDS patients.

Cough was statistically significantly associated with ARDS; RR (95% CI) = 1.8086 (1.0935 to 2.9915), P = 0.0210. Sepsis was associated with 16(42%) of the ARDS patients.

TABLE 1: PATIENTS BY GENDER AND AGE

Variable	ARDS	Non-ARDS	Total
Gender			
Males	21	12	33
Females	17	18	35
Total	38	30	68
Age			
< 18 years	13	2	15
18-30	3	2	5
30-40	2	2	4
40-50	2	2	4
50-60	4	3	7
60+	14	19	33
Total	38	30	68

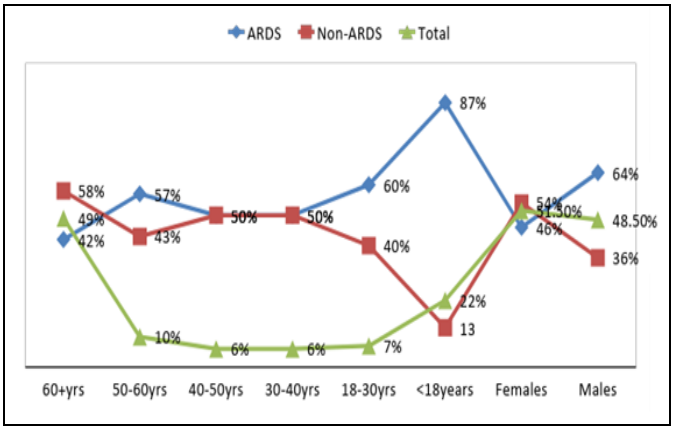

FIG. 1: PATIENTS BY GENDER AND AGE

TABLE 2: PATIENTS BY SYMPTOMS

Variable	ARDS	Non-ARDS	Total
Fever			
Yes	25	9	34
No	13	21	34
Total	38	30	68
Cough			
Yes	27	13	
No	11	17	
Sepsis			
Yes	16	8	24
No	22	22	44
Pneumonia			
Yes	35	15	50
No	3	15	18
H1N1 virus infection			
Yes	10	3	13
No	28	27	55
Coronavirus infection			
Yes	8	2	10
No	30	28	58

The RR (95% CI) = 0.6333 (0.3142 to 1.2764), P = 0.2015. Pneumonia indicated in 35(92%) of the ARDS patients. Pneumonia was statistically significantly associated with ARDS; RR (95% CI) = 1.8421 (1.2727 to 2.6662), P = 0.0012. H1N1 virus infection was found in 10(26%) of the ARDS patients. The RR (95% CI) = 2.6316 (2.6316), P = 0.1135. Coronavirus infection was found in 8(21%) of the ARDS patients. The RR (95% CI) = 3.1579 (0.7234 to 13.7856), P = 0.1262.

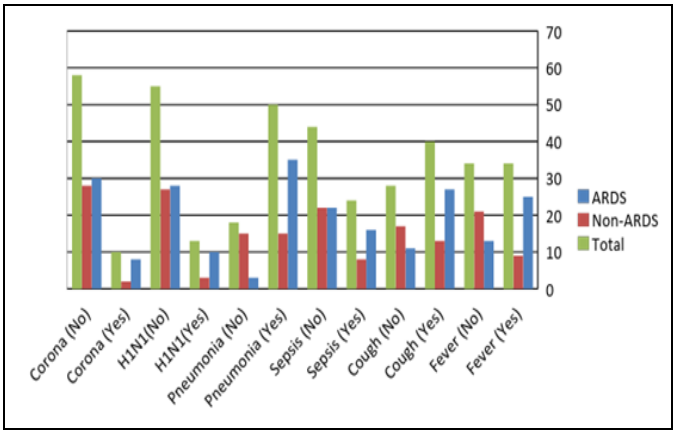

FIG. 2: PATIENTS BY SYMPTOMS

TABLE 3: PATIENTS BY SYMPTOMATIC COMPLICATIONS

Variable	ARDS	Non-ARDS	Total
COPD			
Yes	3	8	11
No	35	22	57
Total	38	30	68
Interstitial lung disease (ILD)			
Yes	8	7	15
No	30	23	53
Cerebral palsy retardation (CPMR)			
Yes	3	3	6
No	35	27	62
Cerebrovascular accident (CVA)			
Yes	4	2	6
No	34	28	62
Cardiac conditions			
IHD	6	6	12
AFib	2	3	5
CHD	3	0	3
CHF	1	0	1
None	26	21	47

Chronic obstructive pulmonary disease (COPD) was identified among 3(8%) of the patients with ARDS. Interstitial lung disease (ILD) was identified among 8(21%) of the patients with ARDS. Cerebral palsy retardation (CPMR) was identified among 3(8%) of the patients with ARDS. Cerebrovascular accident (CVA) was identified among 4(10.5%) of the patients with ARDS. Ischemic heart disease (IHD), Atrial fibrillation (AFib), Coronary heart disease (CHD), and Congestive heart failure (CHF) were identified in

6(16%), 2(5%), 3(8%) and 1(3%) of the patients with ARDS, as shown in **Table 3** and **Fig. 3**.

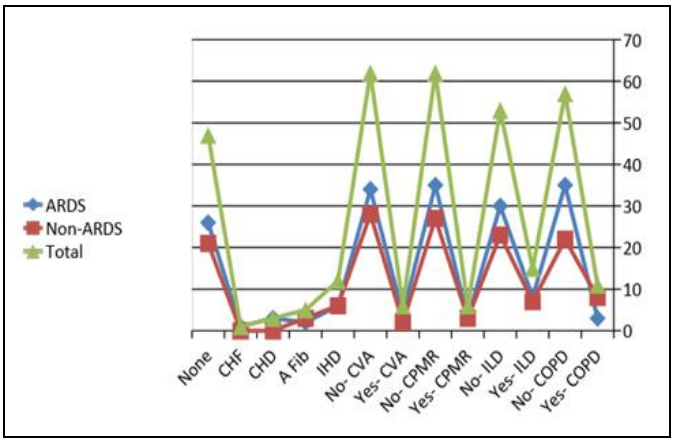

FIG. 3: PATIENTS BY SYMPTOMATIC COMPLICATIONS

DISCUSSION: There is a lack of literature regarding the epidemiology of ARDS from Saudi Arabia, and most epidemiological data are referring to influenza-related virus infection, which is an epidemic during Hajj. Huge population amounts and concentrations at mass gatherings such as the Hajj (Makkah, Saudi Arabia) can vigorously participate in outbreaks of respiratory virus infection by bringing local hot spots for transmission followed by spread to other areas. Outbreaks of respiratory virus infection at mass gatherings designate significant health risks to attendees, host communities and eventually the international population if they support facilitate viral emergence [9]. The prevalence of ARDS was 55.9% among those attending with acute respiratory syndromes in Hail, Region, Northern Saudi Arabia. Almost all studies from Saudi Arabia are reporting acute respiratory syndrome in association with viral infections such as SARS, and MERS-CoV [5, 6]. However, ARDS was reported in association with some infectious [10].

ARDS is statistically significantly associated with older age >60 years and younger generation <18 years. Elderly patients have become an increasingly common proportion of the intensive care unit population. The mortality rate for ARDS has been reported to be very high among elderly patients compared to young [11]. Older age and underlying interstitial abnormalities on chest CT seem to be risk factors for developing ARDS after talc pleurodesis [12]. Improved understanding of the relationship between patient age and acute respiratory distress syndrome (ARDS) development and mortality following traumatic injury may help facilitate the generation of new hypotheses about ARDS pathophysiology and the role of novel treatments to improve outcomes across the age spectrum. Patients ≤4 years and ≥65 years with ARDS experienced the highest-burden of mortality [13]. Acute respiratory distress is one of the most common reasons for emergency visits in children under five y of age [14].

Children ≤4 years were disproportionately affected by ARDS relative to their low underlying mortality following trauma that was not complicated by ARDS. ARDS-associated mortality following trauma has worsened over the past decade, emphasizing the need for new prevention and treatment strategies [13]. In the present study, patients were significantly presented with fever (P = 0.0094). Fever is most probably due to the underlying cause of the ARDS, particularly infectious associated conditions [15]. In the present study, the cough was statistically significantly associated with ARDS; RR (95% CI) = 1.8086 (1.0935 to 2.9915), P = 0.0210. Although the cough isn't a specific symptom for a particular respiratory condition, it was common among this series of patients.

Sepsis was not significantly associated with ARDS, but pneumonia was statistically significantly associated with ARDS; RR (95% CI) = 1.8421 (1.2727 to 2.6662), P = 0.0012. ARDS and hospital-acquired pneumonia (HAP) are major problems of public health in intensive care units (ICUs), occurring in 15% of critically ill patients. Among the factors explaining ARDS development, sepsis is known as a frequent cause. Sepsis, ARDS, and HAP increased morbidity, mortality, length of stay in the ICU, and the overall costs of healthcare [16].

Whereas ARDS is often complicated by nosocomial pneumonia, pulmonary infection is also the most frequent single cause of ARDS. The prevalence of pneumonia during the course of ARDS seems to be unusually high, but whether persons with ARDS are more susceptible to pneumonia or merely have more risk factors remains unknown because of methodological limitations [17]. H1N1 virus infection was found in 26% of ARDS patients. ARDS secondary to

influenza A (H1N1) pdm09 virus is the leading cause of death among this patient population [18]. ARDS complicates up to 55% of influenza-related pneumonia in hospitalized patients and carries a mortality of 40-46% [19]. Coronavirus infection was found in 21% of the ARDS patients. MERS-CoV is transmitted *via* the respiratory tract and causes severe ARDS by infecting lung epithelial cells and macrophages. Macrophages can readily recognize the virus and eliminate it. MERS-CoV infects cells via its Spike (S) glycoprotein that binds on Dipeptidyl-Peptidase 4 (DPP4) receptor present on macrophages [20]. As of Feb 28, 2018, 2182 cases of MERS-CoV infection (with 779 deaths) in 27 countries were reported to WHO worldwide, with most being reported in Saudi Arabia (1807 cases with 705 deaths). MERS-CoV features prominently in the World Health Organization (WHO) blueprint list of priority pathogens that threaten global health security. With 10 million pilgrims visiting Saudi Arabia each year from 182 countries, watchful surveillance by public health systems, and a high degree of clinical awareness of the possibility of MERS-CoV infection is essential [21]. Other conditions such as COPD, ILD, CPMR, CVA and cardiac conditions were found with none significant among cases of ARDS.

CONCLUSION: ARDS is among the most prevalent respiratory syndromes in Northern Saudi Arabia. Older or younger age, male gender, and viral infections are the most frequent factors associated with ARDS. Fever, cough and pneumonia are the most frequent symptoms associated with ARDS.

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CONFLICTS OF INTEREST: Authors declare no conflicts of interest

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