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Incidence Risk and Cumulative Risk of COVID-19 Infection among Healthcare Workers over the First Year of the Pandemic

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ABSTRACT

Objectives

To analyze the spread rate and the cumulative risk of COVID-19 infection among healthcare workers (HCWs) over the first year of the pandemic.

Method

An online, cross-sectional study involved HCWs who were in-service during the first year of COVID-19 crisis, including all healthcare institutions of Jeddah. History and date of COVID-19 infection were collected to estimate the COVID-19-free time, by reference to 03 March 2020, when the first case in Saudi Arabia was identified. Kaplan-Meier survival and Cox regression methods were used to analyze the cumulative risk of COVID-19 infection and the associated factors.

Results

There were three peaks of COVID-19 incidence among HCWs; the highest (7.2%) was in September 2020. The cumulative hazard reached 0.10 by the first trimester, then escalated exponentially during the 3rd trimester to reach a plateau at 0.35. The hazard ratio was independently associated with the HCW's nationality, department affiliation, and receipt of influenza vaccine, as well as the facility type and bed capacity. Receipt of the BCG vaccine in the last year was associated with 40% reduction of the cumulative hazard.

Conclusion

The identified risk factors and high-exposure clusters constitute a weak link in the national management strategy of COVID-19 crisis and highlight the urgent need to reinforce the in-hospital protective measures. Findings from the present study have strong implication for the viability and resilience of the healthcare system during major health crises.

Introduction

The abrupt eruption, rapid spread and persistence of the COVID-19 pandemic represent a serious threat for worldwide health systems to collapse (1–3). The initial phase of the pandemic was characterized by notable shortages of healthcare professionals and personal protective equipment, reduced relative bed capacity both in general and intensive care units, and lack of efficient diagnostic and treatment approaches (4). This resulted in exhaustion and distress among healthcare workers (HCWs) with escalated incidence of depression and burnout (5–9).

In addition to this psychological distress, HCWs are constantly exposed to COVID-19 infection, being at the frontline of the outbreak response. Several international reports communicated worrying numbers of HCWs being infected with COVID-19. This raised further concerns regarding the nosocomial spread of the virus, both regarding the personnel's health and health systems' viability (10–14). One year after the start of the pandemic, and amid the worldwide race for immunization that prioritized HCWs (15–17), the protection of the health systems and their professionals remains a major concern.

In Saudi Arabia, the health care offer is largely covered by the public sector (18). The most updated data (2018) on health manpower affiliated to the Ministry of Health facilities showed a total of 40,084 physicians (1.45 per 1,000 inhabitant), 104,560 nurses (3.10 per 1,000), 3,962 pharmacists (0.12 per 1,000), and 68,655 allied health personal (0.20 per 1,000), distributed on 3,543 utilities (19,20). Furthermore, the Saudi healthcare system is passing through a National Transformation Program (NTP), projecting revolutionary transformations by the year 2030 and requiring huge human resource development (21). Consequently, the knock-one effect of the COVID-19 crisis represents an additional challenge for the achievement of such goal, notably by impeding the attraction of young trainees to the health sector.

Based on these observations, we attempted to understand the epidemic kinetics of COVID-19 among HCWs using an empirical approach to study, by consideration of the amplified cumulative risk of infection and the specific epidemiological parameters within this particular population and setting. It is theorized that the level and rate of an airborne infection spread within a given community are proportional to the levels of exposure and contagiousness, contact duration and efficiency of the immunization and or protection measures that are implemented (22). Thus, the present work aimed at evaluating the risk to Saudi HCWs in airborne outbreaks, thereby inferring the level of safeguard and endurance of the healthcare system against major pandemic and health crises, defining the major weaknesses and drawing beneficial lessons.

This work will be published in two papers with distinct objectives. In this first paper, we estimated of the spread rate of COVID-19 and the cumulative risk of infection among Jeddah HCWs over the first year of the pandemic, and analyzed the associated demographic, professional and baseline clinical factors.

Methods

Design and Setting

A cross-sectional study was conducted between 1st January and 15th February 2021, involving all healthcare institutions of Jeddah, Saudi Arabia. The study protocol was reviewed and approved by the Directorate of Health Affairs, Ministry of Health, Jeddah, Saudi Arabia.

Population and Sampling

The study period was defined as from 03 March 2020, when the first case in Saudi Arabia was identified, to 28 February 2021, date of the end of data collection. The study targeted all individuals who were officially registered and working in any of the MoH, other governmental, private or semi-private health facilities located in Jeddah districts, during the study period. Both care and non-care staff personals were included.

Sample size calculation (N=378) used a single proportion estimate method to detect an unknown COVID-19 infection rate (P=50%) among a total 55,000 HCWs of

Jeddah, with 80% statistical power, 0.05 type 1 error and 95% confidence interval. A convenience sampling method was used to include all valid participations.

Data collection

A comprehensive, structured questionnaire was designed for the purpose of this study, and was divided into 6 parts:"

- **Part 1** included demographic and professional data, such as gender, age, nationality, position, department, type of healthcare facility, bed capacity, etc.
- **Part 2** included baseline health status, such as weight, height, blood group, chronic diseases, smoking status, last year influenza and BCG vaccination status.
- **Parts 3 & 4** included the assessment of occupational and community exposure to COVID-19 infection, respectively; these parts were not included in the present paper and will be presented and analyzed in the second paper of the project.
- **Part 5** included COVID-19 infection and testing status, and comprised 6 items: 1) number of times the participant underwent COVID-19 testing; 2) whether they were diagnosed COVID-19; and in case of positive diagnosis: 3) date of diagnosis, 4) self-assessed severity level; 5) onset symptoms using a predefined list of 13 symptoms; and 6) lieu where the course of illness was spent (quarantine, home isolation, isolation ward, regular ward hospitalization, ICU or other).
- **Part 6** explored the likelihood of being infected from different conceivable persons such as a patient in health facility, colleague, member of the household, etc. Like Parts 3 & 4, this part will also be presented and analyzed in the second paper of the project.

The questionnaire underwent face and content validity by the research team, with the concurrence of an independent methodologist.

Outcome definition

The present study considered two primary outcomes, namely COVID-19 infection rate and COVID-19-free time. Infection rate was calculated as the percentage of participants who have been diagnosed with COVID-19 among the total participants. COVID-19-free time was defined for each participant with positive COVID-19 status as the interval, in weeks, between the effective pandemic onset in Saudi Arabia indicted by the first case reported on the 2nd March 2020 and the date of COVID-19 diagnosis. For participants with negative COVID-19 status, the COVID-19-free time was represented by the whole follow up period = 48 weeks.

Procedure

The questionnaire was edited online using the Google Sheet platform. The contact numbers of all HCWs of Jeddah were obtained from the Directorate of Health Affairs division of Jeddah. A concise message was sent to all eligible individuals, presenting the objectives and importance of the study, specifying the voluntary nature of the participation, and providing the link for the online survey.

Statistical methods

Data was uploaded from the online survey platform as Excel sheet, which was cleaned and recoded, then transferred to SPSS version 21.0 for Windows (SPSS Inc., Chicago, IL, USA) for statistical analysis. Descriptive statistics were used to explore data variables, which were presented as frequency and percentage for categorical variables and mean ± standard deviation (SD) for numerical variables. Kaplan-Meier survival test was used to analyze the cumulative risk of COVID-19 infection among HCWs by

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calculating the mean COVID-19 infection-free time and depicting the cumulative hazard in a hazard function curve. Further, the Kaplan-Meier method was used to analyze the demographic, professional and baseline health parameters as factors of cumulative hazard of COVID-19 infection; results were depicted as mean (95%CI) COVID-19-free time with cumulative risk ratio by quarter, with each parameter category, along with the corresponding Log-rank level. Significant factors were analyzed as independent factors using multivariate Cox-regression; results are presented as hazard ratio (HR) with 95%CI and the corresponding Log-rank level. The null hypothesis was rejected for a *p* value or Log-rank value of <0.05, as applicable.

Results

Participants' characteristics

Of 626 HCWs who received the survey link, 614 (97.8%) have consented and completed the questionnaire. Majority of the participants were female (59.0%), of the care personal (92.2%), and age group 30-49 years (66.8%). Distribution by facility characteristics showed MoH (46.1%) and private (40.6%) hospitals, bed capacity>200 (42.2%), and 32.0% of the participants worked in ER, ICU or isolation ward during the crisis (**Table 1**).

Table 1: Participants' demographic and professional characteristics and their association with COVID-19 infection (N=614)

Parameter	Category	Total, N (%)	COVID-19 infection rate, N (%)	p-value
Gender	Female	362 (59.0)	108 (29.8)	
	Male	252 (41.0)	92 (36.5)	.083
Age (years)	Up to 29	90 (14.7)	26 (28.9)	
	30-39	258 (42.0)	94 (36.4)	
	40-49	152 (24.8)	53 (34.9)	
	50-59	95 (15.5)	24 (25.3)	
	60 and above	19 (3.1)	3 (15.8)	.115
Age-stratified risk exposure	High exposure (30-49 years)	410 (66.8)	147 (35.9)	
	Low exposure (others)	204 (33.3)	53 (26.0)	.014*
Nationality	Saudi Arabia	274 (44.6)	84 (30.7)	
	Philippines	101 (16.4)	30 (29.7)	
	Egypt	105 (17.1)	31 (29.5)	
	India	57 (9.3)	23 (40.4)	
	Sudan	19 (3.1)	7 (36.8)	
	Other	58 (9.4)	25 (43.1)	.312
Nationality-stratified risk exposure	High exposure[§]	134 (21.8)	55 (41.0)	
	Low exposure (others)	480 (78.1)	145 (30.2)	.018*
Facility type	MoH	283 (46.1)	83 (29.3)	
	Non-MoH Governmental	70 (11.4)	49 (70.0)	
	Private	249 (40.6)	62 (24.9)	
	Other	12 (2.0)	6 (50.0)	<.001*
Bed capacity	Less than 50	52 (8.5)	9 (17.3)	
	50-100	103 (16.8)	22 (21.4)	
	100-200	141 (23.0)	37 (26.2)	
	More than 200	259 (42.2)	112 (43.2)	
	Not applicable	59 (9.6)	20 (33.9)	<.001*
Occupation type	Non-care	48 (7.8)	15 (31.3)	
	Care	566 (92.2)	185 (32.7)	.839
Position	Physician	237 (38.6)	71 (30.0)	
	Nurse	197 (32.1)	72 (36.5)	

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	Laboratory personnel	47 (7.7)	12 (25.5)	
	Pharmacist	25 (4.1)	11 (44.0)	
	Physical / Respiratory therapist	29 (4.7)	10 (34.5)	
	Other	31 (5.1)	9 (29.0)	.548
Department	Emergency room (ER)	89 (14.5)	39 (43.8)	
	Intensive care unit (ICU)	63 (10.3)	29 (46.0)	
	Insolation ward	44 (7.2)	22 (50.5)	
	Inpatient - medical ward	56 (9.1)	17 (30.4)	
	Inpatient - Surgical ward	26 (4.2)	8 (30.8)	
	Outpatient clinic	84 (13.7)	22 (26.2)	
	Lab., imaging, Pharmacy, etc.	71 (11.6)	20 (28.2)	
	Other Departments	181 (29.5)	43 (23.8)	.001*
Department-stratified risk exposure	High exposure[⌘]	196 (32.0)	90 (45.9)	
	Low exposure	418 (68.1)	110 (26.3)	<.001*

MoH: Ministry of Health
[§] High-exposure nationalities: India, Sudan, and others than Saudi, Egypt and Philippines.
[⌘] High-exposure departments: Emergency room, intensive care unit, and isolation ward

Table 2: Clinical characteristics of COVID-19 cases (N=200)

Parameter	Category	Frequency	Percentage
Self-assessed severity	Asymptomatic	20	10.0
	Mild	119	59.5
	Moderate	52	26.0
	Severe	9	4.5
Symptoms	Fever	152	76.0
	Sore throat	147	73.5
	Cough	137	68.5
	Myalgia	133	66.5
	Fatigue	126	60.5
	Anosmia	100	50.0
	Loss of appetite	82	41.0
	Shortness of breath	60	30.0
	Diarrhea	58	29.0
	Chills	53	26.5
	Nausea or vomiting	30	15.0
	Headache	17	8.5
	Others	19	9.5
Management	Quarantine	64	32.0
	Home isolation	103	51.5
	Isolation ward	21	10.5
	Regular ward hospitalization	6	3.0
	ICU	3	1.5
	Other	3	1.5

Baseline health-related data showed a high percentage of overweight (40.6%) and obesity (27.4%), besides hypertension (17.9%), asthma (10.9%), and diabetes (10.4%). The most common blood group was O+ (34.7%), followed by A+ (27.0%). There were 17.4% and 16.4% current cigarettes and shisha smokers, respectively (**Table 3**).

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Table 3: Participants' baseline health status and their association with COVID-19 infection (N=614).

Parameter	Category	Total, N (%)	COVID-19 infection rate, N (%)	p-value
BMI class (kg/m^2)	Underweight (<18.5)	13 (2.1)	1 (7.7)	
	Normal (18.5-24.9)	184 (30.0)	58 (31.5)	
	Overweight (25-29.9)	249 (40.6)	89 (35.7)	
	Obesity I (30-34.9)	127 (20.7)	41 (32.3)	
	Obesity II (35-39.9)	35 (5.7)	10 (28.6)	
	Obesity III (40+)	6 (1.0)	1 (16.7)	.321
Chronic diseases	Hypertension	110 (17.9)		
	Asthma	67 (10.9)		
	Diabetes	64 (10.4)		
	Heart diseases	26 (4.2)		
	Other atopic/autoimmune/rheumatic diseases	23 (3.7)		
	Immune deficiency	19 (3.1)		
	Anxio-depressive disorder	13 (2.1)		
	Liver disease	11 (1.8)		
	Cancer	8 (1.3)		
	CKD	8 (1.3)		
	Dialysis	6 (1.0)		
	Other chronic disease	39 (6.4)		
Number of chronic diseases	None	392 (63.8)	122 (31.1)	
	One	144 (23.5)	57 (39.6)	
	Two or more	78 (12.7)	21 (26.9)	.094
Blood group	A+	166 (27.0)	50 (30.1)	
	A-	18 (2.9)	13 (72.2)	
	B+	129 (21.0)	41 (31.8)	
	B-	17 (2.8)	7 (41.2)	
	O+	213 (34.7)	62 (29.1)	
	O-	20 (3.3)	6 (30.0)	
	A2	42 (6.8)	18 (42.9)	
	Do not know	9 (1.5)	3 (33.3)	.016*
Blood group	High risk (A-, B- and A2)	77 (12.5)	38 (49.4)	
	Low risk (others)	537 (87.5)	159 (30.1)	.001*
Smoking status	Non-smoker	436 (71.0)	133 (30.5)	
	Ex-smoker	71 (11.6)	14 (19.7)	
	Current smoker	107 (17.4)	53 (49.5)	.001*
Shisha smoker	No	513 (83.6)	158 (30.8)	
	Yes	101 (16.4)	42 (41.6)	.035*
Influenza vaccine last year	No	146 (23.8)	33 (22.6)	
	Yes	468 (76.2)	167 (35.7)	.003*
BCG vaccine last year	No	249 (40.6)	111 (44.6)	
	Yes	365 (59.4)	89 (24.4)	<.001*

MoH: Ministry of Health

Estimation of the cumulative incidence of COVID-19 infection

A total 200 HCWs were diagnosed COVID-19 over the pandemic period, resulting in a cumulative incidence of 32.6% (95%CI=28.9, 36.4%). There was no significant difference between non-care (31.3%) and care (32.7%) staffs (p=0.839) (**Results not presented in Tables**). The highest monthly incidence rate was observed during September (7.2%). Overall, there were three peaks of incidence, in April-May, July,

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and September-October. The evolution of the monthly incidence rate and the cumulative incidence are depicted in **Figure 1a**.

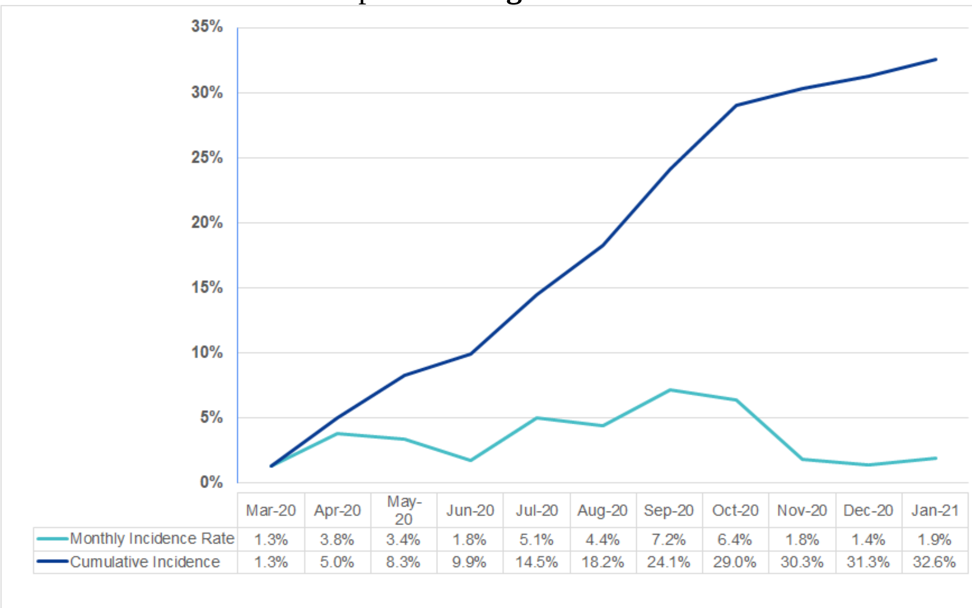

Figure 1a: Monthly incidence rate and cumulative incidence of COVID-19 infection among healthcare workers in Jeddah, Saudi Arabia, from March 2020 to January 2021

Estimation of cumulative risk of COVID-19 infection among HCWs using the Kaplan-Meier hazard function

The Kaplan-Meier hazard function curve is depicted in **Figure 1b**. The mean COVID-19 infection-free time was 40.9 (95%CI= 39.7 – 42.0) weeks, and the cumulative hazard nearly doubled each quarter, starting from 0.08 by the end of the 1st quarter, i.e., 12 weeks after the first KSA case, and increasing to 0.18 at the 2nd and 0.36 at the 3rd quarter, then flattening to reach 0.38 by the end of the 4th quarter.

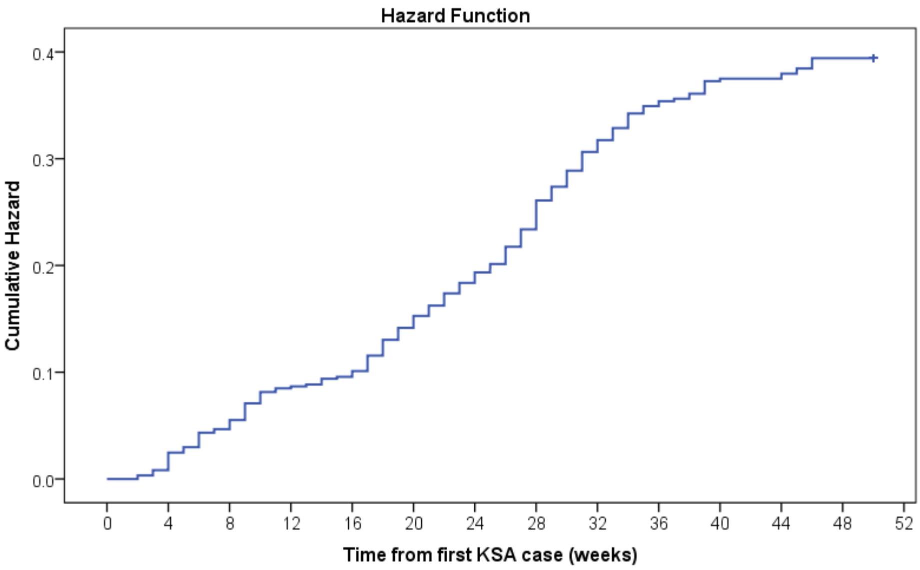

Figure 1b: Cumulative risk of COVID-19 infection among healthcare workers in Jeddah, over 48 weeks from the first case in Saudi Arabia (02 March 2020)

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Factors associated with the cumulative risk of COVID-19 infection among HCWs

The cumulative risk of COVID-19 infection was significantly greater among age group 30-49 years (Log-Rank=0.011), Group A nationalities including India, Sudan, and Others than Saudi, Egypt and Philippines (Log-Rank=0.007), participants working in non-MoH governmental hospitals (Log-Rank<0.001), facilities with bed capacity>200 (Log-Rank<0.001), or high-risk departments (Log-Rank<0.001). Further, current smoking (Log-Rank<0.001), shisha smoking (Log-Rank=0.021), and having taken influenza vaccine last year (Log-Rank=0.006) were also associated with greater risk of COVID-19 infection, while BCG vaccine was associated with reduced cumulative risk (Log-Rank<0.001). Estimations of the mean infection-free time as well as the cumulative risk in the 4 quarters, by factor categories, are depicted in **Table 4**, while the hazard function curves by factors are depicted in **Figure 2**.

Table 4: Demographic, professional and baseline health determinants of cumulative risk of COVID-19 infection among healthcare workers in Jeddah (N=614)

Parameter	Category	Mean COVID-Free time (weeks)	Cumulative risk by quarter[‡]				Log-Rank
			Q1 (12w)	Q2 (24w)	Q3 (36w)	Q4 (50w)	
Gender	Female	41.8 (40.3, 37.7)	0.08	0.17	0.30	0.35	
	Male	39.5 (37.6, 41.4)	0.10	0.20	0.42	0.45	.074
Age	**30-49 years**	39.7 (38.3, 41.2)	0.10	0.21	0.39	0.44	
	others	43.1 (41.3, 44.9)	0.06	0.11	0.26	0.30	.011*
Nationality	**Group A**[§]	37.2 (34.4, 40.1)	0.15	0.31	0.50	0.52	
	Group B	41.9 (40.6, 43.1)	0.07	0.15	0.31	0.37	.007*
Facility type	MoH	41.4 (39.7, 43.1)	0.09	0.19	0.30	0.34	
	Non-MoH Gov.	31.0 (27.4, 34.7)	0.19	0.36	1.10	1.20	
	Private	42.9 (41.2, 44.5)	0.06	0.12	0.25	0.28	
	Other	43.6 (38.9, 48.2)	0.0	0.0	0.19	0.70	<.001*
Bed capacity	<50	45.0 (41.8, 48.3)	0.06	0.08	0.17	0.19	
	50-100	43.4 (40.8, 46.0)	0.06	0.15	0.23	0.25	
	100-200	43.1 (41.0, 45.2)	0.05	0.12	0.28	0.30	
	More than 200	37.5 (35.5, 39.5)	0.14	0.28	0.51	0.57	
	Not applicable	42.0 (38.9, 45.1)	0.0	0.18	0.34	0.42	<.001*
Occupation	Non-care	40.8 (39.6, 42.0)	0.11	0.18	0.27	0.38	
	Care	41.5 (37.3, 45.6)	0.08	0.19	0.36	0.40	.816
Department[⁂]	High risk	36.8 (34.5, 39.1)	0.14	0.28	0.55	0.62	
	Low risk	42.8 (41.5, 44.0)	0.07	0.15	0.29	0.31	<.001*
Chronic disease	None	41.1 (39.7, 42.6)	0.09	0.19	0.33	0.38	
	One	39.7 (37.3, 42.0)	0.07	0.18	0.44	0.50	
	Two or more	41.6 (38.3 45.0)	0.11	0.17	0.31	0.31	.140
Blood group	A-, B- or A2	37.3 (33.8, 40.8)	0.14	0.24	0.51	0.69	
	Others	41.4 (40.1, 42.6)	0.08	0.18	0.34	0.37	.001*
Smoking status	Nonsmoker	41.5 (40.2, 42.8)	0.06	0.16	0.32	0.36	
	Ex-smoker	44.2 (41.4, 47.1)	0.02	0.13	0.21	0.21	
	Current smoker	35.9 (32.7, 39.1)	0.22	0.27	0.54	0.70	<.001*
Shisha smoking	No	41.5 (40.2, 42.7)	0.07	0.17	0.34	0.37	
	Yes	37.8 (34.5, 41.0)	0.16	0.27	0.48	0.54	.021*
Influenza vaccine last year	No	43.3 (41.2, 45.5)	0.05	0.13	O.24	0.26	
	Yes	40.1 (38.7, 41.4)	0.1	0.20	0.39	0.45	.006*
BCG vaccine last year	No	37.4 (35.3, 39.3)	0.17	0.26	0.48	0.59	
	Yes	43.2 (41.9, 44.9)	0.03	0.14	0.27	0.28	<.001*

[‡] Approximative values estimated from the Kaplan-Meier cumulative hazard curves

§ Group A nationalities: India, Sudan, and Others than Saudi, Egypt and Philippines.
⌘ High-risk departments: Emergency room, intensive care unit, and isolation ward
MoH: Ministry of Health
* Statistically significant difference (Log-rank<0.05)

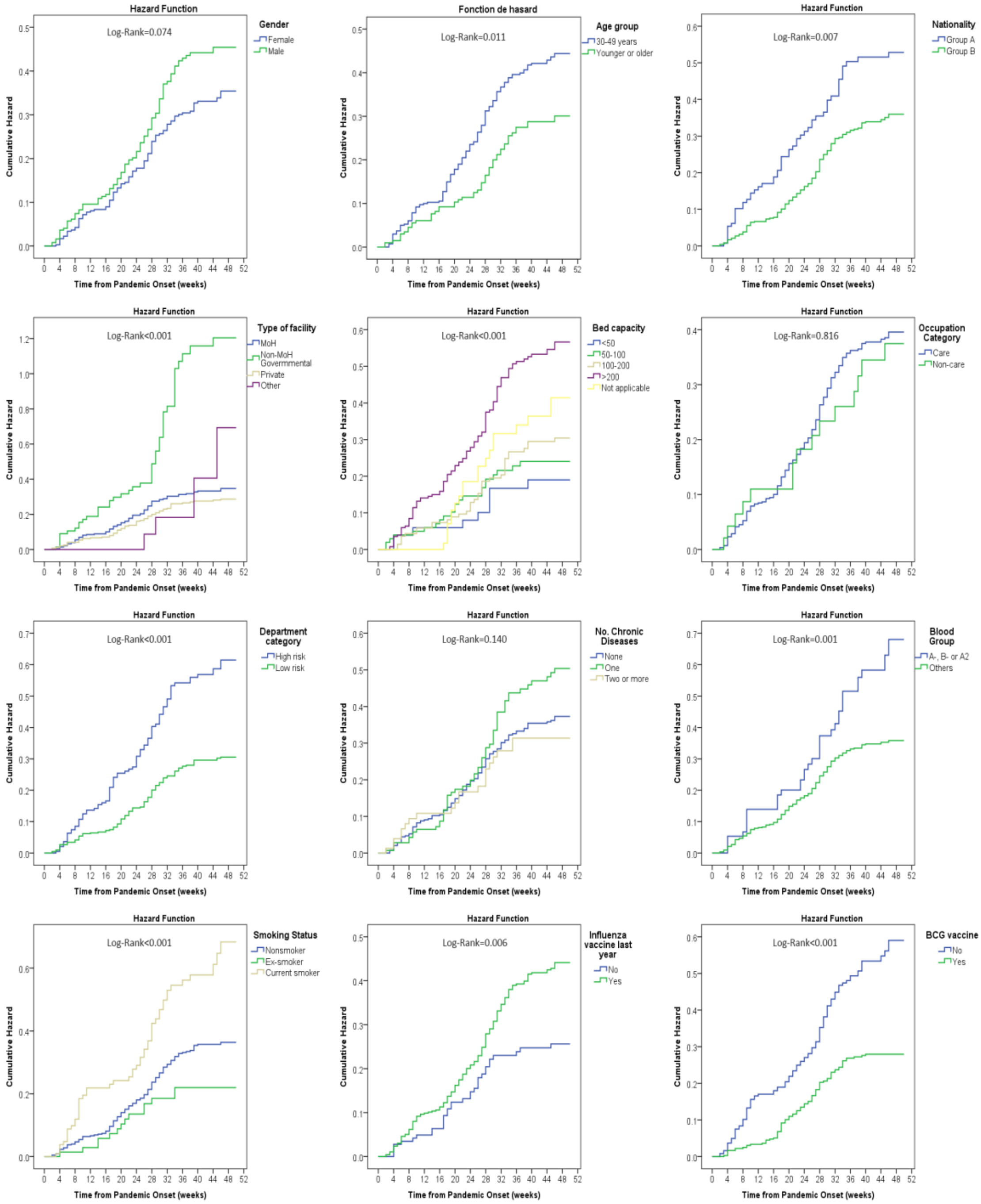

Figure 2: Factors associated with cumulative hazard of COVID-19 infection among healthcare workers in Jeddah, over 48 weeks from the first case in Saudi Arabia (02 March 2020).

Predictors of cumulative risk of COVID-19 infection among HCWs

The cumulative risk of COVID-19 infection was independently associated with Group A nationalities (HR=1.6, Log-Rank=0.009), non-MoH governmental hospital (HR=3.2, Log-Rank<0.001), bed capacity>200 (HR=1.9, Log-Rank=0.035), influenza vaccine last year (HR=1.5, Log-Rank=0.030), and BCG vaccine (HR=0.6, Log-Rank=0.002) (**Table 5**).

Table 5: Independent factors associated with cumulative risk of COVID-19 infection among healthcare workers in Jeddah (N=614)

Parameter	**Category**	**HR**	**95%CI**		**Log-Rank**
Age	**30-49 years**	1.4	1.0	1.9	.070
	others	Ref			
Nationality	**Group A[§]**	**1.6**	**1.1**	**2.2**	**.009***
	Group B	Ref			
Facility type	MoH	Ref			<.001*
	Non-MoH Gov.	**3.2**	**2.2**	**4.6**	**<.001***
	Private	1.0	0.7	1.5	.979
	Other	1.2	0.5	3.3	.692
Bed capacity	<50	Ref			.231
	50-100	1.8	0.8	4.3	.153
	100-200	1.6	0.8	3.6	.214
	>200	**2.3**	**1.1**	**4.8**	**.035***
	Not applicable	2.1	0.9	5.0	.097
Department	**High risk[‡]**	**1.9**	**1.4**	**2.6**	**<.001***
	Low risk	Ref			
Blood group	A-, B- or A2	1.3	0.9	1.8	.226
	Others	Ref			
Smoking status	Nonsmoker	Ref			0.072
	Ex-smoker	0.6	0.4	1.1	0.115
	Current smoker	1.3	0.9	1.9	0.178
Shisha smoking	No	Ref			
	Yes	1.4	1.0	2.1	0.082
Influenza vaccine last year	No	Ref			
	Yes	**1.5**	**1.1**	**2.3**	**0.030***
BCG vaccine last year	No	Ref			
	Yes	**0.6**	**0.5**	**0.8**	**0.002***

Test: Multivariate Cox-Regression (Event=COVID-19 infection).
HR: Hazard-ratio; 95%CI: 95% confidence interval
[§] Group A nationalities: India, Sudan, and others than Saudi, Egypt or Philippines
[‡] High-risk departments: Emergency room, intensive care unit, and isolation ward
MoH: Ministry of Health; Gov.: governmental
* Statistically significant difference ($p<0.05$)

Discussion

Relevance and summary of findings

The specific risk among HCWs of COVID-19 infection results principally from the repeated exposure to symptomatic and asymptomatic carriers of the SARS-CoV-2 in relatively high-risk situations, in addition to their regular exposure to the virus in the community. The present cross-sectional study suggests that nearly one-third of HCWs in Jeddah have been infected with SARS-CoV-2 during the first year of the COVID-19 pandemic, with no difference between care and non-care staffs. There were three peaks of incidence, with the highest monthly incidence of 7.2% observed in September 2020. The cumulative hazard reached 0.10 by the end of the first trimester, then escalated exponentially during the 3rd trimester to end up with a plateau at approximately 0.35 by the last trimester. Several risk factors have been identified to

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be increasing the cumulative hazard, while adjusted analysis showed that the hazard ratio independently increased for HCWs from nationalities other than Saudi, Egyptian and Philippines, those working in non-MoH governmental hospitals, high-bed capacity facilities, or high-exposure departments, and those who have received influenza vaccine last year. On the other hand, receipt of the BCG vaccine in the last year was demonstrated to be a protective factor against COVID-19, associated with 40% reduction of the cumulative hazard of infection.

Significance of the cumulative hazard estimates and COVID-19-free time analysis

The survival analysis-based model used in the present study showed that the cumulative hazard increased exponentially starting from the second semester, which corresponds to the second wave of the pandemic. Together with the estimate of the mean COVID-19-free time, which was found to be approximately 9 months, may be indicative of the viability and robustness of the health system. It also showed that the period between the 5th and 8th month, namely July-October, constituted a turnover in the pandemic kinetics among HCWs, and marks a break point with the pandemic figure in the general population.

Comparison of infection rate among HCWs with that in the Saudi general population and limitation of the corresponding finding

On 28th February, date of the endpoint of the present study, the cumulative incidence rate of COVID-19 in the Saudi population reached 1.07% with a total 377,383 cases (23–25). This is far from reflecting the 32.6% cumulative incidence rate found in HCWs in the present study. It is likely that, due to the very low response rate the study design has induced a considerable selection bias, where HCWs who were infected were more engaged to participate in the study. It is unfortunately impossible to provide a more accurate estimate using the present data, which reduces the external validity of this specific objective, namely the infection rate among HCWs, which is probably overestimated. A more accurate estimate could be obtained from the analysis of COVID-19 records of occupational health services, notably by using a cluster sampling to do the same.

However, by comparing the epidemic curves of HCWs versus the general population (see **Figure 1** and (23,24)), the two cumulative incidence curves seem to match perfectly; whereas regarding the new cases, that of HCWs curve (monthly incidence rate) appears to be offset with respect to that of the general population. That is, after a small peak in April-May 2020 observed in both populations, the daily incidence in the general population reached its highest rate in June 2020, while this month corresponds to a net decline of the incidence in HCWs. Subsequently, the incidence rate in the general population declined progressively from July to September 2020, whereas this period corresponds to an upsurge in HCWs, where a decline was only observed from October 2020 on. This may be explained by the presence of two overlapping pathways of the virus dissemination among HCWs including community-acquired and the nosocomial/occupational infection. More detailed analysis will be carried out in the second paper from the present work to address this point.

COVID-19 among HCWs and its impact on health system worldwide

Majority studies that were concerned with COVID-19 infection among HCWs were carried out in the early phase of the pandemic. During a systematic screening campaign, a Qatari study conducted at 14 inpatient hospitals from the Hamad Medical Corporation (HMC) between 10 March and 24 June 2020 reported 10.6% RT-PCR positive results among 16,912 tested HCWs (26). This concords with 9.9%

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cumulative incidence rate found in the present study and indicates the substantially high incidence of COVID-19 in HCWs in the region.

In the other continents, a meta-analysis that included 7 Chinese, 3 American and one Italian studies at the early phase of the pandemic (up to April 2020) showed that HCWs represented 4.2 to 17.8% of the total COVID-19 cases depending on the country. On the other hand, the same study showed that both the incidence of severe cases (~10% versus 29.4%) and mortality (0.3% versus 2.3%) were significantly lower among HCWs by reference to the population respectively (27). By contrast, the present study showed only 4.5% of severe cases among infected HCWs and only 1.5% required an ICU admission, while mortality was not analyzable using the present design.

An Australian study that analyzed all the declared cases of hospital COVID-19 outbreaks and COVID-19 positive HCWs, up to 8 July 2020, reported an infection rate less than 0.1% among HCWs versus 0.034% among the general population. This demonstrated that even with such a low COVID-19 incidence in the general population, HCWs are exposed to a 2.7-fold risk of being infected. Further, authors reported that the hospitals caused the closure of 1 out 21 concerned hospitals, and the quarantining of 1,200 HCWs (28). This shows the large impact of COVID-19 on the health systems, assuming greater impact in high-incidence countries. By comparison, we observed 14.5% incidence rate of COVID-19 among HCWs in July 2020 versus less than 0.7% in the Saudi general population, representing more than 20-fold risk among HCWs.

Another figure was reported from the data of 592 symptomatic HCWs, originating from an occupational health service in Massachusetts, US, which showed 14.0% positive SARS-CoV-2 RT-PCR cases between 9 March and 15 April 2020 (29). By considering the same period, this rate is very high compared to the cumulative incidence rate of 5.0% observed in the present study by the end of April 2020. Over the same period of April 2020, a British study that tested 1,000 asymptomatic HCWs showed a positivity rate of 3% (30), which is lower than that observed in the present study. Nonetheless, this data demonstrated the role of asymptomatic carriage in occupational transmission of COVID-19, which may induce a shadow pandemic within the health institutions. In a single-center study from Spain that included 1,911 HCWs, 213 out of 652 symptomatic ones tested positive using RT-PCR on 30 April 2020, which represented 11.1% overall prevalence and 32.7% of the symptomatic and tested ones (31).

Another longitudinal study from 4 teaching hospitals in the UK monitored the COVID-19 molecular (PCR testing) and serological (anti-Spike IgG) statuses of 12,541 initially asymptomatic HCWs over 31 weeks, i.e., from 23 April to 30 November 2020. Authors observed a baseline seropositivity rate as high as 9.4%, which rose to 10.1% by the end of the study accounting for 88 additional cases of seroconversion. Additionally, 1.7% of HCWs who were seronegative throughout follow up tested PCR positive, resulting in an overall estimated incidence of 11.7% (32). Comparison of these findings with the corresponding figures from the present study raise two observations. On the one hand, the baseline seroprevalence of 9.4% is significantly higher that the cumulative incidence of 5.0% found in April 2020 in the present study. On the other hand, the endpoint estimates of 11.7% is significantly lower than the 30.3% cumulative incidence rate found in the same period in the present study. This may suggest that the highest contamination rate among HCWs in the UK occurred in the onset of the pandemic, while in Saudi it is occurred

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subsequent to the second wave, i.e., between July and October. It is, however, worth noting that the UK study included only asymptomatic HCWs, while reduces the conclusiveness of this comparison.

Likewise, a systematic review and meta-analysis studied the prevalence and risk factors of COVID-19 among 230,398 HCWs from 97 observational studies that were published before 8 July 2020. Using RT-PCR (46 studies including 75,859 HCWs), the prevalence of COVID-19 among HCWs ranged from 0.4% in Spain to 57.1% in New York City, US, and the pooled prevalence using the same diagnostic method was estimated as 11%, 19% and 5%, overall, in symptomatic only, and in asymptomatic individuals respectively. By considering seroprevalence studies (28 studies including 27,445 HCWs), the percentage of seropositive COVID-19 cases was 7%, for a test sensitivity ranging between 75% and 100% and specificity higher than 80% (33). These figures are comparable to the 14.5% cumulative incidence found in the present study in July 2020 and reflect a worldwide consistent epidemic kinetics in the first 6 months of the pandemic.

Factors increasing the cumulative hazard of COVID-19 among HCWs

The present study identified some high-risk/high-exposure clusters that may constitute a weak link in the national management strategy of health crises similar to COVID-19. Accurate identification of such clusters and risk factors would enable targeted auditing and reinforcement of the implemented protective measures. The greatest hazard ratio of COVID-19 infection was observed among HCWs affiliated to non-MoH governmental facilities, who would be inferentially exposed to a 3.2 odd risk of infection over the first year, by reference to their peers working in MoH facilities. However, private hospitals showed a level of exposure that is similar to MoH institutions.

The second greatest hazard ratio of COVID-19 infection was observed among HCWs affiliated to high bad capacity facilities or high-risk departments including ER, ICU and isolation ward, who were respectively exposed to 2.3- and 1.9-fold risk by references to their counterparts. By assuming consistent adherence to the protective measures, the risk of occupational COVID-19 infection is conceivably proportional to the qualitative and quantitative level of exposure to potentially infectious individuals. By contrast with our findings, a Spanish study showed lower infection rates (9.1%) among HCWs from departments classified as high exposure to COVID-19 including ER, ICU and medical COVID-19 units, versus those classified as medium exposure level such as outpatient clinic (14.1%) and medical no COVID-19 units (16.1%) (31). Another study from Los Angeles, US, reported that 46.6% of a total 5,458 COVID-19 positive HCWs were working in long-term care facilities, and 27.7% in hospitals, while those working in outpatient clinics represented only 6.9% (34).

Further, the HCW's nationality was independently predictive for the risk of COVID-19. That is, Indian, Sudanese and nationalities other than Saudi, Egyptian and Philippines HCWs had 60% additional cumulative risk of contracting COVID-19. This finding may be explained by several factors and confounders, which could be addressed on analysis of the occupational and community exposures. In the previously cited Qatari study, Indian nationality represented nearly 51% of the COVID-19 cases among HCWs (26). Similarly, a retrospective study from the US showed that HCWs of African American or Hispanic descent had 2.8 times higher incidence than their non-Hispanic white peers (35). These observations demonstrate the importance of assessing sociodemographic factors in addressing the risk of COVID-19 infection among HCWs, beside the assessment of the professional factors.

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BCG vaccine as a protective factor against COVID-19?

Interestingly, BCG vaccination was found to be an independent protective factor against COVID-19 infection, associated with 40% reduction in the cumulative hazard. Several international reports continue to support such negative association between BCG vaccination and the COVID-19 incidence, severity or mortality. Substantial decreases in COVID-19 related mortality and severity were observed in countries applying systematic BCG vaccination policies by reference to those without such policy (36,37). The suspected mechanism lies in the non-specific immune response elicited by the BCG vaccine, which translates into what is called "trained immunity" and which previously demonstrated protection against various pathogens other than *Mycobacterium Tuberculosis*, notably viruses such as yellow fever virus, influenza A (H1N1), herpes virus (HSV), respiratory syncytial virus (RSV), and the human papilloma virus (HPV). This trained immunity effect of BCG vaccine confers cross-protection via several immunological mechanisms, and in the case of COVID-19 the mechanism is likely mediated by enhanced reactivity of CD4+ and CD8+ T-cell to SARS-CoV-2. However, no properly designed clinical trials were conducted so far to confirm the causal relationship (38–40).

Study Quality and limitations

The major limitation that may impacts the external validity of the present study is the low response rate probably associated with a selection bias favoring COVID-19 HCWs. Such an issue exposes to overestimation of the cumulative incidence. On the other hand, non-inclusion of COVID-19 death cases among HCWs represents a risk of underestimation, that would probably be of lesser extent, in absolute value, compared with the previously discussed overestimation. Otherwise, the pattern of the epidemic kinetics including and the calculations of the hazard ratios associated with the different parameters could be inferred to the target population and guide further investigations and corrective measures to reinforce the weak links of the health system.

Conclusion

Nearly one-third of included HCWs in Jeddah have contracted COVID-19 during the first year of the pandemic, with no difference between care and non-care staffs. There were three peaks of incidence, with the highest monthly incidence of 7.2% observed in September 2020, and the cumulative hazard increased exponentially as of August 2020, corresponding to the second wave of the pandemic with a one-month offset with respect of the epidemic kinetics in the general population. Several risk factors and high-exposure clusters have been identified, which may constitute a weak link in the national management strategy of health crises similar to COVID-19 and highlight the urgent need to audit and reinforce the implemented protective measures to enhance the resilience of the national health system.

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