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The incidence of moderate and severe COVID-19 at Zagazig University Hospitals: A single center experience in Egypt

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ABSTRACT

Background: Coronavirus Disease 2019 (COVID-19) is a paramount public health issue. The true statistics about COVID-19 in Egypt are veiled. **Aim:** To determine the incidence rate of moderate and severe SARS-CoV-2 infection among the patients seeking admission to Zagazig University Hospitals (ZUH), Egypt based on the chest Computed Tomography (CT) COVID-19 Reporting and Data System (CO-RADS) radiological criteria. **Methods:** All patients aged ≥ 18 years old seeking admission to ZUH between January 1st and March 31st, 2021, were eligible for enrollment in the study if they performed non-enhanced chest CT. Assessment of clinical, laboratory, and chest CT CO-RADS radiological criteria for each patient was carried out. The patients were defined to have moderate or severe COVID-19 if they met CO-RADS 4 or 5 radiological criteria, respectively, in association with the clinical and/or laboratory criteria. **Results:** A total of 5549 subjects were enrolled in the study. The total number of moderate and severe COVID-19 cases diagnosed at ZUH during January 2021 was 434/1827 with a monthly incidence rate of 23.75; 95% CI (21.9-25.8) per 100,000 of the population. The total number of moderate and severe COVID-19 cases during February 2021 was 215/1622 with a monthly incidence rate of 13.25; 95% CI (11.7-15). During March, the total number of moderate and severe COVID-19 cases was 416/2100 with a monthly incidence rate of 19.8; 95% CI (18.2-21.6). **Conclusion:** The incidence rate of moderate and severe COVID-19 infection at ZUH is in parallel with the national COVID-19 incidence reports.

Introduction

By 20th November 2021, the new coronavirus termed "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2) had infected about 257 million individuals globally resulting in 5.14 million fatalities [1]. By the time of writing this manuscript, Egypt is ranked 80th in the globe in terms of COVID-19 infection [2].

Egypt was the first African nation to declare a confirmed COVID-19 case on February

14, 2020. According to the official website of the Egyptian Ministry of Health (MOH), which is dedicated to the news of COVID-19 epidemic in Egypt, a total of 208,876 laboratory-confirmed SARS-CoV-2 infections were recorded between February 14, 2020, and April 9, 2021, including 12,362 deaths (5.92% case fatality rate) [3]. However, Dr. Khaled Abdel Ghaffar, Egypt's Minister of Higher Education and Scientific

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Research, confirmed that the number of Egyptians infected with the virus was substantially higher than what the government had stated [4].

The Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) assay was first used to confirm the diagnosis of COVID-19. However, its reported sensitivities ranging from 42% and 83%. Multiple false negative findings have been documented in individuals with typical COVID-19 clinical and radiological evidence. Therefore; the role of chest CT for the diagnosis of COVID-19 was evolved [5]. The 7th Chinese Novel Coronavirus Pneumonia Diagnosis and Treatment Plan incorporated chest CT imaging into the criteria that clinically define COVID-19 [6].

There have been several attempts to standardize CT reporting of suspected COVID-19. A "COVID-19 standardized reporting" working group was established and the authors developed a standardized assessment scheme for pulmonary involvement of COVID-19 given the nomenclature CO-RADS for COVID-19 Reporting and Data System. This scheme proved to work well in clinical practice [7].

Ash Sharqia Governorate is the third among all Egyptian governorates concerning high population density with a population of 8 million citizens according to the latest official available data [8]. There are no electronic databases in all public Egyptian hospitals. As a result, there is a dearth of information on the epidemiology of COVID-19 in Egypt, making it difficult to estimate the disease's actual incidence rate. The current study's objective was to ascertain the incidence of moderate and severe SARS-CoV-2 infection at ZUH, Ash Sharqia Governorate, Egypt, during the second wave of the pandemic using the CO-RADS scheme.

Methods

a) Study setting & design

This prospective cohort study was carried out at the Emergency (A&E) and Outpatients departments of Zagazig University Hospitals (ZUH), Ash Sharqia Governorate, Egypt between January 1st and March 31st, 2021. Being a very busy tertiary care facility and in the context of the absence of patients' electronic databases, the working team could not be able to manually calculate the incidence of moderate and severe COVID-19 cases at the ZUH for more than three months.

b) Study population

Inclusion criteria: All patients (aged ≥ 18 years, males or females) seeking admission to ZUH through the Emergency and/or Outpatient departments were eligible for enrollment in the study after performing a non-contrast chest CT scan. Exclusion criteria: a) age < 18 years, b) patients refused to perform the chest CT scan.

c) The institutional screening program (the study tool)

By the beginning of the epidemic in Egypt, ZUH established a radiological-based screening service for all patients seeking hospital admission. All participants were subjected to thorough history taking, clinical, laboratory, and radiological assessment by non-contrast chest CT scan.

d) Definition of COVID-19 cases

Any person who exhibited at least one of the following clinical symptoms (fever, cough, shortness of breath, sudden onset of anosmia, ageusia, or dysgeusia) in addition to radiological evidence compatible with COVID-19 by non-contrast chest CT scan (CO-RADS 4&5) was defined to have COVID-19 infection, regardless of whether there was close contact with a confirmed COVID-19 case in the 14 days prior to the symptoms or not [9].

It was impossible to employ the SARS-CoV-2 nucleic acid or antigen in the clinical specimen as a confirmatory laboratory criterion because neither was available in the Emergency or Outpatient departments. According to institutional rules, access to SARS-CoV-2 RT-PCR and/or antigen was only permitted after admission to the quarantine hospital.

Patients were divided into three categories based on the criteria listed in the Egyptian MOH care protocol for COVID-19 [10]. Mild cases were defined as those in which there was no radiological evidence of pneumonia but there were clinical symptoms, leucopenia, or lymphopenia (not included in the current study). Patients exhibiting clinical symptoms, leucopenia, lymphopenia, and/or radiological signs of pneumonia were categorized as having a moderate illness. Blood oxygen saturation at rest of $\leq 92\%$, partial pressure of arterial blood oxygen (PaO₂)/oxygen concentration (FiO₂) 300 mmHg, or respiratory distress with a respiratory rate >30 /min were used to diagnose severe cases. Critically ill refers to all severe instances that progressed to shock, respiratory failure requiring mechanical ventilation, or other organ failures.

e) CT technique and image analysis

All CT scans were performed using a 128 detector scanner (Philips Healthcare Ingenuity). All patients were scanned on supine position during single deep-inspiration breath-hold. No contrast medium was administered. Each CT scan was analyzed by two independent radiographers; both agreed on the CO-RADS classification for each chest CT scan.

f) COVID-19 Reporting and Data System (CO-RADS)

CO-RADS is a categorical assessment scheme for chest CT in patients suspected of COVID-19, representing the level of suspicion for pulmonary involvement. The level of suspicion increases from very low (CO-RADS 1) to very high (CO-RADS 5). According to Prokop et al. original's work, CO-RADS 1 represents a very low probability of COVID-19 infection; CO-RADS 2, low probability; CO-RADS 3, equivocal/unsure probability; CO-RADS 4, high probability; and CO-RADS 5, very high probability [7]. Two additional categories respectively encode a technically insufficient examination (CO-RADS 0) and RT-PCR-proven SARS-CoV-2 infection at the time of examination (CO-RADS 6).

g) Ethical approval

The protocol of the research was approved by Zagazig University- Faculty of Human Medicine Research Ethics Committee (ZU-IRB No: 9266) and followed the Declaration of Helsinki guidelines for ethical principles in medical research. All patients were informed and signed written consent.

Statistical analysis

Data management was performed using the MedCalc software (version 20.113). Incidence rate (per 100.000) was calculated as the sum of new cases categorized to have clinical symptoms, laboratory evidence, and CO-RADS 4&5 criteria by chest CT divided by the size of population at risk. The population at risk was defined as all patients came to the emergency and outpatient departments seeking admission to ZUH.

Results

A total of 5549 patients were examined at the A&E and outpatient departments of ZUH between January 1st and March 31st, 2021. Based on the clinical symptoms and the CO-RADS classification scheme, the total number of moderate and severe COVID-19 cases was (1065/5549, 19.2%) whereas, the total number of non-suspected cases was (4484/5549, 80.8%).

During January 2021, a total of 1,827 patients sought admission to ZUH. Of them, 434 (23.8%) were diagnosed to have moderate and severe COVID-19 and 1,393 (76.2%) were non-suspected cases as shown in **figure (1)**. During February 2021, a total of 1622 patients came to the A&E and outpatient departments for admission. Of them, 215 (13.3%) were classified as moderate and severe COVID-19 cases and 1407 (86.7%) cases were none suspected to have COVID-19 as shown in **figure (2)**. During March 2021, a total of 2100 patients were examined at the A&E and outpatient departments. Of them, 416 (19.8%) were diagnosed to have moderate and severe COVID-19 infection and 1684 (80.2%) were non-suspected cases as shown in **figure (3)**. A graphical comparison of the total number of moderate and severe COVID-19 cases and non-suspected cases during the study period is shown in **figure (4)**. Daily numbers of moderate and severe COVID-19 cases at ZUH during the study period are shown in the supplementary figures.

The incidence rate of moderate and severe COVID-19 at ZUH during January was 23.75; 95% CI (21.9-25.8) per 100.000 inhabitant whereas it was 13.25; 95% (11.7-15) during February. The incidence rate during March was 19.8; 95% CI (18.2-21.6). The daily, weekly and monthly moderate and severe COVID-19 incidence rates during the study period are shown in **tables (1,2 &3)**. Graphical comparison between the monthly incidence rates is shown in **figure (5)**.

Table 1. Incidence of moderate and severe COVID-19 at ZUH during January 2021.

Date	COVID-19 Cases (N)	Non-suspected Cases (N)	Total (N)	Daily incidence/100.000
1 st	28	61	89	31.46
2 nd	17	32	49	34.69
3 rd	46	70	116	39.65
4 th	23	79	102	22.54
5 th	11	39	50	22
6 th	20	45	65	35.71
7 th	9	14	23	39.13
Total	154	340	494
Weekly Incidence	31.17 ; 95% CI (27.3-35.5)			
8 th	3	12	15	20
9 th	16	42	58	27.58
10 th	26	67	93	27.95
11 th	32	77	109	29.35
12 th	12	23	35	34.28
13 th	28	94	122	22.95
14 th	8	36	44	18.18
Total	125	351	476
Weekly Incidence	26.3; 95% CI (22.6-30.5)			
15 th	2	3	5	40
16 th	25	98	123	20.32
17 th	11	67	78	14.1
18 th	20	88	108	18.51
19 th	7	23	30	23.33
20 th	24	92	116	20.69
21 th	1	15	16	6.25
Total	90	386	476
Weekly Incidence	18.9 ; 95% CI (15.7-22.8)			
22 th	2	5	7	28.57
23 th	16	70	86	18.6
24 th	13	62	75	17.33
25 th	17	89	106	16
26 th	2	23	25	8
27 th	12	66	78	15.38
28 th	3	1	4	75
Total	65	316	381
Weekly Incidence	17; 95% CI (13.7-21.3)			
Monthly Incidence	23.75; 95% CI (21.9-25.8)			

Table 2. Incidence of moderate and severe COVID-19 at ZUH during February 2021.

Date	COVID-19 Cases (N)	Non-suspected Cases (N)	Total (N)	Daily incidence /100.000
29 th	0	0	0	N/A*
30 th	16	84	100	16
31 th	14	64	78	17.94
1 st	10	70	80	12.5
2 nd	2	22	24	8.33
3 rd	9	60	69	13
4 th	4	19	23	17.39
Total	55	319	374
Weekly Incidence	14.7; 95% CI (11.5-18.8)			
5 th	2	5	7	28.5
6 th	17	64	81	20.98
7 th	9	57	66	13.63
8 th	15	78	93	16.12
9 th	2	24	26	7.69
10 th	12	75	87	13.79
11 th	2	20	22	9
Total	59	323	382
Weekly Incidence	15.4; 95% CI (12.2-19.5)			
12 th	1	4	5	20
13 th	17	78	95	17.89
14 th	8	74	82	9.75
15 th	10	91	101	9.9
16 th	2	23	25	8
17 th	11	81	92	11.95
18 th	3	19	22	13.63
Total	52	370	422
Weekly Incidence	12.3; 95% CI (9.5-15.9)			
19 th	0	3	3	N/A
20 th	11	72	83	13.25
21 th	13	77	90	14.44
22 th	10	93	103	9.7
23 th	4	26	30	13.33
24 th	9	101	110	8.18
25 th	2	23	25	8
Total	49	395	444
Weekly Incidence	11; 95% CI (8.5-14.4)			
Monthly Incidence	13.25; 95% CI (11.7-15)			

*N/A= Not Available

Table 3. Incidence of moderate and severe COVID-19 at ZUH during March 2021.

Date	COVID-19 Cases (N)	Non-suspected Cases (N)	Total (N)	Daily incidence /100,000
26 th	1	5	6	16.66
27 th	12	96	108	11.1
28 th	8	54	62	12.9
1 st	30	85	115	26
2 nd	13	23	36	36.11
3 rd	23	63	86	26.7
4 th	4	26	30	13.3
Total	91	352	443
Weekly Incidence	20.5; 95% CI (17.1-24.7)			
5 th	2	5	7	28.57
6 th	24	98	122	19.67
7 th	13	64	77	16.88
8 th	28	80	108	25.92
9 th	9	26	35	25.71
10 th	23	81	104	22.11
11 th	16	34	50	32
Total	115	388	503
Weekly Incidence	22.86; 95% CI (19.5-26.8)			
12 th	1	5	6	16.66
13 th	27	99	126	21.42
14 th	21	71	92	22.82
15 th	16	89	105	15.23
16 th	0	0	0	NA
17 th	29	63	92	31.5
18 th	5	23	28	17.85
Total	99	350	449
Weekly Incidence	22; 95% CI (18.5-26.2)			
19 th	1	2	3	33.3
20 th	4	34	38	10.52
21 th	8	52	60	13.33
22 th	13	67	80	16.25
23 th	8	26	34	23.52
24 th	9	62	71	12.67
25 th	7	15	22	31.8
Total	50	258	308
Weekly Incidence	16.2; 95% CI (12.6-20.1)			
26 th	2	19	21	9.52
27 th	7	74	81	8.64
28 th	7	68	75	9.33
29 th	26	86	112	23.2
30 th	2	20	22	9
31 th	17	69	86	19.7
Total	61	336	397
Weekly Incidence	15.4; 95% CI (12.1-19.3)			
Monthly incidence	19.8; 95% CI (18.2-21.6)			

Figure 1. Total No. of moderate and severe COVID-19 cases in comparison to unsuspected cases at ZUH during January 2021.

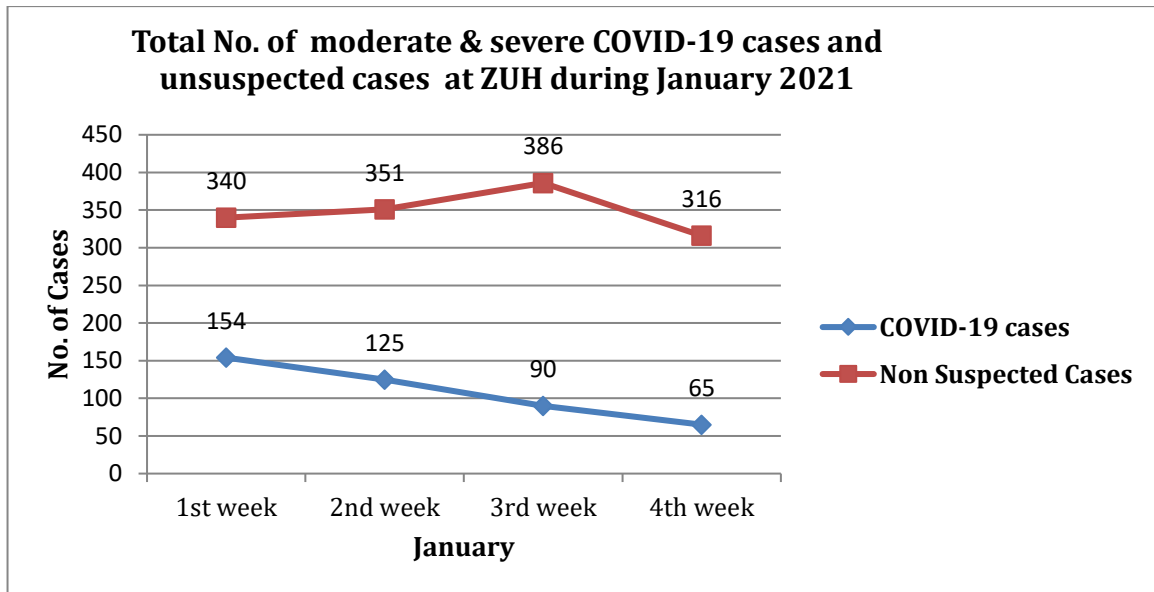


Figure 2. Total No. of moderate and severe COVID-19 cases in comparison to unsuspected cases at ZUH during February 2021.

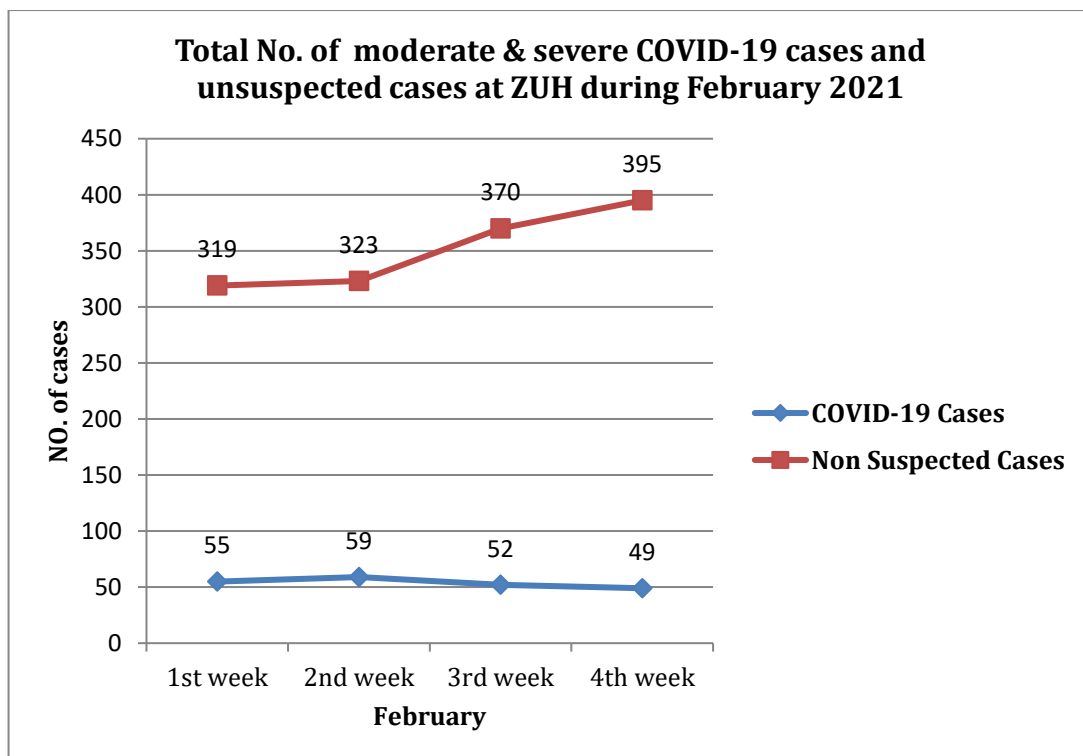


Figure 3. Total No. of moderate and severe COVID-19 cases in comparison to unsuspected cases at ZUH during March 2021.

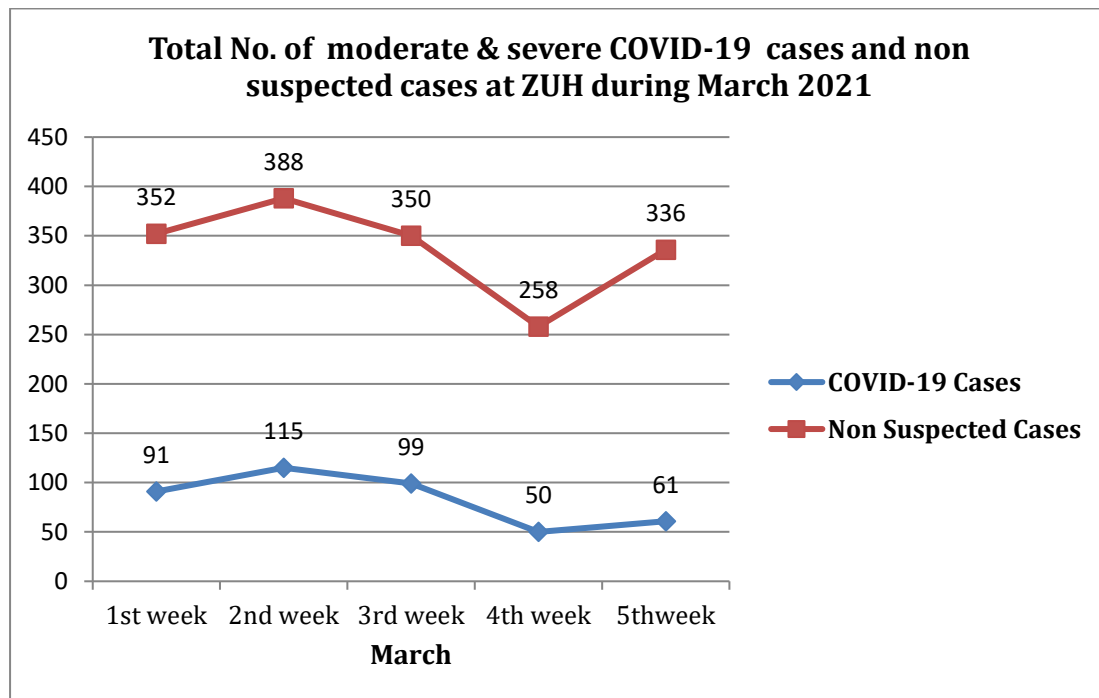


Figure 4. Total No. of moderate & severe COVID-19 cases and unsuspected cases at ZUH during the whole study period.

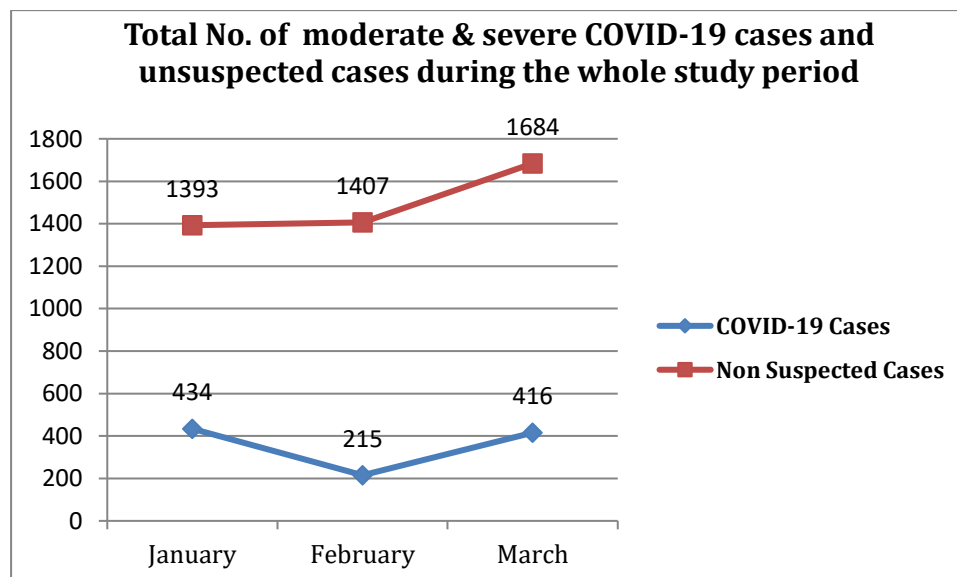
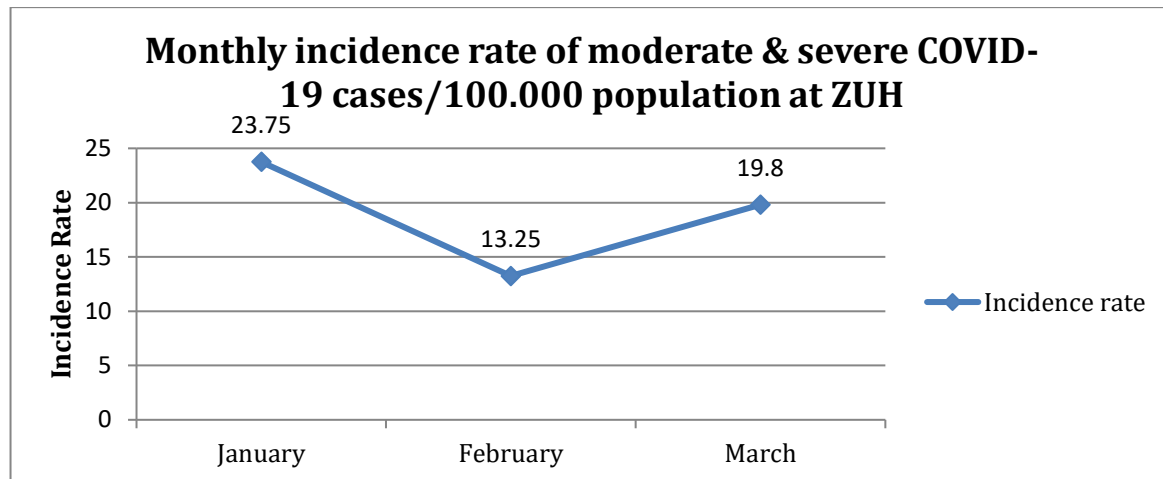


Figure 5. Monthly Incidence rate of moderate & severe COVID-19 cases at ZUH during the study period.

Discussion

In Egypt, the COVID-19 reported cases are consensually believed to be underreported [11]. Thus, we tried to estimate the real incidence of moderate and severe COVID-19 infection, based on the radiological CO-RADS scheme, at ZUH, Ash Sharqia governorate, Egypt.

To our knowledge, the only available study in literature discussing the positivity rates of SARS-CoV-2 in Egypt is that conducted by Girges et al. [12]. However, their study was based on SARS-CoV-2 RT-PCR and antibody testing rather than the CO-RADS scheme. The research was conducted at Ain Shams University Hospitals and found that out of a total of 4,313 patients, 4,008 had the RT-PCR test and 2,951 had the antibody assay, respectively. SARS-CoV-2 RT-PCR positivity rate was 3.84%, and SARS-CoV-2 antibody sero-prevalence was 29.82%. There are no other similar studies in the literature to compare with. Thus, the official data reported by the Egyptian MOH regarding moderate and severe COVID-19 confirmed cases from January 1st to March 31st 2021 was used in the current study [13].

Because of the E&A policies at ZUH, which operate only at full strength on specific days of the week, and therefore the number of cases on cold days will be less not because of the low level of infection, but due to the lack of reception of cases, and accordingly, it was more accurate to use IR as a parameter for making the assessment.

Since the population of the Arab Republic of Egypt is 100 million, and by generalizing the results of the current study and by comparing it with the national incidence reports of moderate and

severe COVID-19 as shown in the supplementary table. It is clear that the results of the current study are in agreement with the national reports about moderate and severe COVID-19 incidence rates.

However, there are many claims that the officially published COVID-19 figures are underrated. **Medhat & El Kassas** discussed these claims and suggested that the lower rate of COVID-19 infection in Egypt in comparison to other countries may be attributed to the national quarantine measures, hot weather, early BCG vaccination, SARS-CoV-2 subtypes, and fewer screening tests [14].

Looking into the details, the Egyptian MOH has established a COVID-19 task force to control the country's preventive, containment, and mitigation efforts. Egypt's authorities shut down schools and major social gatherings like weddings and funerals [15]. It should be noted that the current study was conducted during the period of this comprehensive closure between the beginning of January- Mid of March 2021.

Concerning the influence of the weather on COVID-19 transmission, **Wang et al.** hypothesized that different temperatures could have a substantial impact on the SARS-CoV-2 transmission. From January 20 to February 4, 2020, they gathered the total number of COVID-19 confirmed cases globally and estimated the daily average, minimum, and maximum temperatures. They were the first to discover that various temperatures had a major influence on COVID-19 transfer from person to person [16]. In the main, low temperature and low humidity have been linked to the transmission of other coronaviruses [17-19]. Furthermore, cold meteorology is likely to weaken the physiological

responses and decrease human immunological function and thereby raising the risk of infectious diseases [20,21]. Consequently, the dramatic drop in the number of cases reported in our study may be attributed to both comprehensive closure and moderate weather in comparison to other countries.

From other perspective, Egypt incorporated Bacille Calmette-Guérin (BCG) vaccination in mandatory vaccination programs early since 1974 [22]. BCG is a live attenuated vaccine against Mycobacterium Bovis. It has been demonstrated to cause non-specific immunological effects, leading to an enhanced response against other non-mycobacterial species. Furthermore, the BCG vaccine increases the production of pro-inflammatory cytokines, particularly IL-1 β , which have antiviral properties [23]. As a result, Egypt's low COVID-19 infection can be traced in part to the country's early BCG immunization. In Contrast, nations that have never implemented universal vaccination regimes (Italy, the United States, and the Netherlands) reported higher rates of COVID-19 infection and death. Interestingly, nations that implemented the BCG vaccination programs late in the twentieth century, such as Iran, had also higher rates of infection and death, which might be attributed to an unprotected older population [24].

Finally, while no genetic investigations on SARS-CoV-2 variants have been conducted in Egypt, it is generally known that the S type has a lower transmission rate than the L type, and the low number of cases in Egypt may indicate a less aggressive subtype of COVID-19 [25].

Implications of the study

This study provides a better understanding of the true incidence of moderate and severe COVID-19 cases at ZUH, Egypt.

Limitations of the study

(1) The cases were diagnosed based on clinical symptoms, laboratory investigations, and chest CT scans (2) SARS-CoV-2 RT-PCR or antigen testing was not accessible at E&A or outpatient departments (3) The cases were not followed up after being transferred from the E&A or outpatient departments (4) The factors affecting the occurrence of the disease were not evaluated in this study (5) Being a hospital-based study, the data still may not reflect all cases in the community who sought medical advice at other public or private facilities.

Conclusion

This study highlights the true incidence of moderate and severe COVID-19 at ZUH, As Sharqia Governorate, one of the highest-density population governorates in Egypt. The findings of this research revealed a satisfactory agreement with the officially published COVID-19 figures. The study also highlights some justifications that explain the lower incidence rates of COVID-19 infection reported in Egypt in comparison to other countries.

Authors' contribution

Dina M. Ali is the principle investigator responsible for the concept, study design, analysis and interpretation of data, writing the draft, and final revision of the manuscript. Khaled Raafat is attributed to critical revision of the manuscript. Lamiaa G. Zake is attributed to collection of data, interpretation of data, and final revision of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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Availability of data

Available from the corresponding author upon request.

Supplementary materials

Supplementary figures and table are available at: DOI: 10.6084/m9.figshare.21311400

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List of abbreviations

A&E department: Accident and Emergency department; **CO-RADS:** Corona Virus Disease Reporting and Data System; **COVID-19:** Corona Virus Disease-2019; **CT:** Computed Tomography; **SARS-CoV-2:** Severe Acute Respiratory Syndrome Corona Virus 2; **RT-PCR:** Real Time Polymerase Chain Reaction; **MOH:** Ministry of Health; **ZUH:** Zagazig University Hospitals.

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