Co-infection with SARS-CoV-2 and influenza A/H1 in a patient seen at Influenza like-Illness surveillance site in Egypt: Case-report

Manal Fahim, Hanaa Abu El Sood Ghonim, Wael H. Roshdy, Amel Naguib, Nancy Elguindy, Mohamad AbdelFatah, Mohamed Hassany, Amira Mohsen, Salma Afifi, Alaa Eid

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of September 7, 2020, a total of 27,314,629 confirmed COVID-19 cases and 893,474 related deaths have been reported worldwide (WHO 2020). In Egypt, a total of 99,863 confirmed COVID-19 cases and 5,530 related deaths have been reported as of September 7, 2020 (WHO 2020).
Influenza like Illness (ILI) sentinel surveillance in Egypt started in year 2000 in 8 sentinel sites geographically distributed all over the country. Patients presenting to the outpatient clinics in the participating hospitals with fever and cough within the last 10 days are required to provide throat swabs to be kept in viral transport media (VTM), stored in nitrogen tank at -80 ?C and shipped on a weekly basis to the Central Public Health Lab (CPHL) in Cairo for testing for influenza types and subtype by reverse transcription polymerase chain reaction (RT-PCR). Patients' demographic and clinical data are collected in a special database that is regularly analyzed. Reports with the rate of influenza positivity and prevalent influenza type and subtype is provided to decision makers and relevant stakeholders on a weekly basis. Since the beginning of the COVID-19 pandemic, Egypt Ministry of Health and Population (MoHP) requested adding SARS-CoV-2 to the testing panel in all ILI surveillance sites.
Early in the pandemic, CPHL was the only laboratory approved by MoHP for SARS-CoV-2 testing. Accordingly testing for influenza was on hold starting from October 2019 and specimens collected from ILI patients were archived at -70°C for subsequent testing when possible. As the number of COVID-19 patients in Egypt started to decline in August 2020, CPHL set up to test the archived specimens collected by ILI sites for influenza type and subtype, and SARS-CoV-2 by RT-PCR (Viasure Sars-CoV-2 Real Time PCR Detection Kit (CerTest Biotec, Spain). A recent report from CPHL released on 16th August 2020 identified a case with mixed SARS-CoV-2 and Flu-A/H1 viruses infection. This report aims at describing how the case was identified and the patient's demographic and clinical characteristics and outcomes.

Objective: This report aims at describing how the case was identified and the patient's demographic and clinical characteristics and outcomes.

Methods: Influenza like Illness (ILI) sentinel surveillance in Egypt started in year 2000 in 8 sentinel sites geographically distributed all over the country. Patients presenting to the outpatient clinics in the participating hospitals with fever and cough within the last 10 days are required to provide throat swabs to be kept in viral transport media (VTM), stored in nitrogen tank at -80 ?C and shipped on a weekly basis to the Central Public Health Lab (CPHL) in Cairo for testing for influenza types and subtype by reverse transcription polymerase chain reaction (RT-PCR). Patients' demographic and clinical data are collected in a special database that is regularly analyzed. Reports with the rate of influenza positivity and prevalent influenza type and subtype

is provided to decision makers and relevant stakeholders on a weekly basis. Since the beginning of the COVID-19 pandemic, Egypt Ministry of Health and Population (MoHP) requested adding SARS-CoV-2 to the testing panel in all ILI surveillance sites.

Results: of ILI patients testing indicated that more than 80% of cases were negative for both SARS-CoV-2 and influenza. Broader viral testing might be needed to identify the etiology particularly if it would affect patient treatment (Kondo 2020).

Conclusions: treatment.
Discussion
Dual infection of corona viruses and Influenza A viruses was reported before (Jiang 2020). During the current COVID-19 pandemic, co-infection of SARS-CoV-2 and influenza A/H1 was reported from many countries including China, Italy, Iran, and Japan (Wu 2020, D'Abramo 2020, Hashimi 2020, Kondo 2020, Azekawa 2020).
The case reported from Egypt was a young female whereas most of the patients reported from other countries were older ages. In a mini-review that describes 37 patients with SARS-CoV-2 and influenza coinfection by D'Abramo et al., it was found that 66.7% of patients were ?50 years of age, and 56.5% were males (D'Abramo 2020).
Most of the cases with co-infection reported from other countries had prolonged course ofthe disease, with all of them admitted to hospital (Wu 2020, D'Abramo 2020, Hashimi 2020, Kondo 2020, Azekawa 2020). While the case reported from Egypt had mild symptoms, she was detected during routine ILI surveillance activities. She had short course of 4 days with home treatment, that is why she had no radiology or blood testing done. Her contacts even had milder symptoms, so they did not seek any medical advice.
Most of the cases with co-infection reported had predisposing factors reducing their immunity and many of them required mechanical ventilation and/or ICU admission. It was found that more than 60% of patients with co-infection had comorbidities, 33% needed artificial ventilation, and 29% were admitted to ICU5. Up-to date the case reported from Egypt is the only one with mild upper respiratory symptoms reported from any country. This could be related to her age and gender in addition to the absence of pre-disposing comorbidities.

Conclusion: Egypt is reporting a case of SARS-CoV-2 and influenza A/H1 co-infection with mild ILI symptoms. This finding suggested that co-infection can occur in people of younger ages with no comorbidities. The report showed that patient immunity can overcome both infections leading to full recovery in a short period with no need to medical procedures. ILI surveillance proved effective in detection of the viral causes of patients with ILI symptoms. Broadening of the testing panel is recommended especially if it could guide case management.
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Abstract:

Background: Influenza like Illness (ILI) sentinel surveillance in Egypt started in year 2000 in 8 sentinel sites geographically distributed all over the country. In response to the COVID-19 pandemic, SARS-CoV-2 was added to the viral testing panel by PCR for the first two patients with ILI seen at one of the sentinel sites. We report the first SARS-CoV-2 and influenza A/H1 virus co-infection with mild symptoms detected through routine influenza like-illness surveillance (ILI) in Egypt.

Objectives: This report aims at describing how the case was identified and the patient's demographic and clinical characteristics and outcomes.

Methods: The case was identified by the central public health laboratory staff who contacted the ILI sentinel surveillance officer at Ministry of Health. The case was contacted through phone call. Detailed information about patient clinical picture, course of disease and outcome. Patient's contacts were investigated for acute respiratory symptoms, disease confirmation and outcome.

Results: Among 510 specimens collected from patients with ILI symptoms from October 2019 to August 2020. Of them 61 (12.0%) were COVID-19 positive and 29 (5.7%) were positive for influenza including 15 (51.7%) A/H1, 11 (38.0%) A/H3, and 3 (10.3%) Flu-B. A 21-year-old female was confirmed as SARS-CoV-2 and influenza A/H1 virus co-infection. She had high fever of 40.2°C and mild respiratory symptoms that resolved within two days with symptomatic treatment. All her five family contacts had mild respiratory symptoms 2-3 days after exposure to the confirmed case and symptoms resolved without treatment or investigations.

Conclusions: The case highlights the possible occurrence of co-infection in younger and healthy people who might resolve the infection rapidly. We emphasize the usefulness of surveillance system for detection of viral causative agent(s) of ILI and recommend the broadening of testing panel especially if it could guide case management.

Introduction

Coronavirus disease 2019 epidemic situation:

COVID-19 is caused the virus SARS-CoV-2. As of September 7, 2020, a total of 27,314,629 confirmed COVID-19 cases and 893,474 related deaths have been reported worldwide [1]. In Egypt, a total of 99,863 confirmed COVID-19 cases and 5,530 related deaths have been reported as of September 7, 2020 [2].

Egypt Influenza like Illness Surveillance

Influenza like Illness (ILI) sentinel surveillance in Egypt started in year 2000 in 8 sentinel sites geographically distributed all over the country. Patients presenting to the outpatient clinics in the participating hospitals with fever and cough within the last 10 days are required to provide throat swabs to be kept in viral transport media (VTM), stored in nitrogen tank at -80 ^{0}C and shipped on a weekly basis to the Central Public Health Lab (CPHL) in Cairo for testing for influenza types and subtype by reverse transcription polymerase chain reaction (RT-PCR). Patients' demographic and clinical data are collected in a special database that is regularly analyzed. Reports with the rate of influenza positivity and prevalent influenza type and subtype is provided to decision makers and relevant stakeholders on a weekly basis.

The modifications to ILI surveillance scheme during COVID-19 pandemic

Since the beginning of the COVID-19 pandemic, Egypt Ministry of Health and Population (MoHP) requested all patients with acute respiratory symptoms at all governmental hospitals to be assessed by the Emergency Department (ED). Accordingly, ILI surveillance teams were requested to enroll the first two patients with ILI symptoms every day from the ED and follow the usual surveillance methodology in data and sample collection. MoHP requested to add SARS-CoV-2 to the testing panel in all ILI surveillance sites.

Early in the pandemic, CPHL was the only laboratory approved by MoHP for SARS-CoV-2 testing. Because of resources constraints testing for influenza was on hold starting from October 2019 and specimens collected from ILI patients were archived at -70°C for subsequent testing when possible. As the number of COVID-19 patients in Egypt started to decline in August 2020, CPHL set up to test the archived specimens collected by ILI sites.

Study objectives

On 16th August 2020 CPHL notified the MoHP surveillance department of a case with mixed SARS-CoV-2 and Flu-A/H1 viruses infection. This report aims at describing how the case was identified

and the patient's demographic and clinical characteristics and outcomes.

Methods:

ILI surveillance methods: Case detection

The influenza virological surveillance was implemented in Egypt 2000 in 8 outpatient clinics in 6 governorates all over Egypt. Subjects enrolled in the virological surveillance (2-3 ILI subjects per day, 6 days a week) are interviewed for their demographic information. WHO case of ILI is used to recruit patients including Abrupt onset of fever ≥38º C with respiratory manifestations of cough with onset within last 10 days [3].

While testing the routine ILI samples, CPHL staff noticed a case of co-infection of SARS-CoV-2 and influenza A/H1 confirmed by PCR.

Case investigation

They contacted surveillance officer who investigated the case through phone call. Patient clinical picture, disease course, severity risk factors, other clinical investigations and disease outcome was investigated for the case and her contacts. Surveillance data are entered in real-time online database at MoHP, laboratory data are entered at CPHL to be merged automatically to the surveillance data. ILI data from October 2019 to August 2020, was extracted and analyzed for influenza and SARS-CoV-2 and co-infection.

Laboratory and clinical investigations

Nasopharyngeal swab was collected from the patient and Nucleic acid extraction for clinical sample were done using the chemagic™ 360 instrument (Perkin Elmer, Waltham, Massachusetts, USA). Detection of SARS-CoV-2 RNA (ORF1 ab) was performed using Viasure Sars-CoV-2 Real Time PCR Detection Kit (CerTest Biotec, Zaragoza, Spain). The RT-PCR runs were done in triplicate and according to manufacturer's recommendations and the positive samples was confirmed for the SARS-CoV-2 using (cobas® 6800,ROCHE, Switzerland) .While influenza A(H1) was tested by real time PCR using CDC protocol [4].A complete blood picture (CBC) and Computed tomography (CT) of the chest were performed.

Results:

ILI surveillance virological results

Among 510 specimens collected from patients with ILI symptoms from February to August 2020, 29 (5.7%) were positive for influenza. Of those, 15 (51.7%) had A/H1, 11 (38.0%) A/H3, and 3 (10.3%) Flu-B. The first case of COVID-19 in Egypt was announced on the 14th of February, whereas the ILI

surveillance caught its first COVID-19 case two weeks later announcing the beginning of community transmission of the disease in Egypt. Of the 510 specimens tested, 61(12.0%) were COVID-19 positive (Figure 1). One case was confirmed for both SARS-CoV-2 and influenza A/H1.

Case investigation results

The case presented to the outpatient clinic of one of the ILI surveillance sites that serves Helwan -a semi-urban area in Cairo- on the 18th of May 2020. She was 21-year-old female student complaining of fever, cough, fatigue, and malaise for two days with no other symptoms or associated comorbidities. She presented with high fever of 40.2°C, her chest was free on auscultation. Blood picture was normal and computerized tomography (CT) chest was clear indicating that the patient had no lower respiratory tract infection. The patient was swabbed and sent home for treatment, she was given symptomatic treatment in the form of antipyretic, antitussive and oral Cefadroxil 2g per day. Symptoms persisted for two days followed by full recovery. At home, no isolation was done for the case and four out of her five family contacts had mild respiratory symptoms 2-3 days after exposure to the confirmed case. Secondary cases included the two parents (both are 49 years of age), two brothers (9 and 16 years old) all recovered within 2-3 days, except the father who was having hypertension and recovered in two weeks. All her contacts did not seek healthcare and recovered without treatment.

Laboratory and clinical investigation results

The patient was positive by RT-PCR for both SARS-CoV-2 and influenza A/H1. The main Ct value for SARS-CoV-2 N gene was 16.1 and for ORF 1ab was 14.2(CerTest Biotec, Spain), also the main Ct value for SARS-CoV-2 ORF 1ab gene was 14.9 and for E gene was 15.6 using (cobas® 6800, ROCHE, Switzerland) as a confirmatory method, while the main Ct value for influenza A was 32.6 and for swFluA was 32.2, and for swH1was 31.6. CBC was normal and chest CT imaging was clear.

Discussion

Co-infection of SARS-CoV-2 and influenza A/H1

This study illustrates the characteristics of the first case of SARS-CoV-2 and influenza A/H1 co-infection with mild ILI symptoms in Egypt and highlights the benefit of surveillance system for co-detection of respiratory viruses.

Co-infection of previous corona viruses and Influenza A viruses was reported before [5]. During the current COVID-19 pandemic, co-infection of SARS-CoV-2 and influenza A/H1 was reported from

case studies conducted in many countries including China, Italy, Iran, and Japan [6-9].

Predominating viral cause

The abrupt symptoms of high fever and short incubation period of secondary and the mildness and short course of disease may suggest influenza was the main causative agent [10]. Interestingly the Ct-values in the specimen of this patients indicates that the viral load of SARS-CoV-2 infection is much higher than influenza A/H1. Studies suggest that the viral load of SARS-CoV-2 peaks around symptom onset or a few days later [11]. This could suggest that influenza infection occurred earlier and competitively suppressed replication of SARS-CoV-2 [12].

How Egypt case compares to cases reported from other countries

Demographics

The case reported from Egypt was a young female whereas most of the patients reported from other countries were older ages. In a mini-review that describes 37 patients with SARS-CoV-2 and influenza coinfection by D'Abramo et al., it was found that 66.7% of patients were ≥50 years of age, and 56.5% were males [7].

Disease course and severity

Most of the cases with co-infection reported from other countries had prolonged course of the disease, with all of them admitted to hospital [6-10]. While the case reported from Egypt had mild symptoms, she was detected during routine ILI surveillance activities. She had short course of 4 days with home treatment, her CBC and CT chest were normal. Her contacts even had milder symptoms, so they did not seek any medical advice.

Predisposing factors

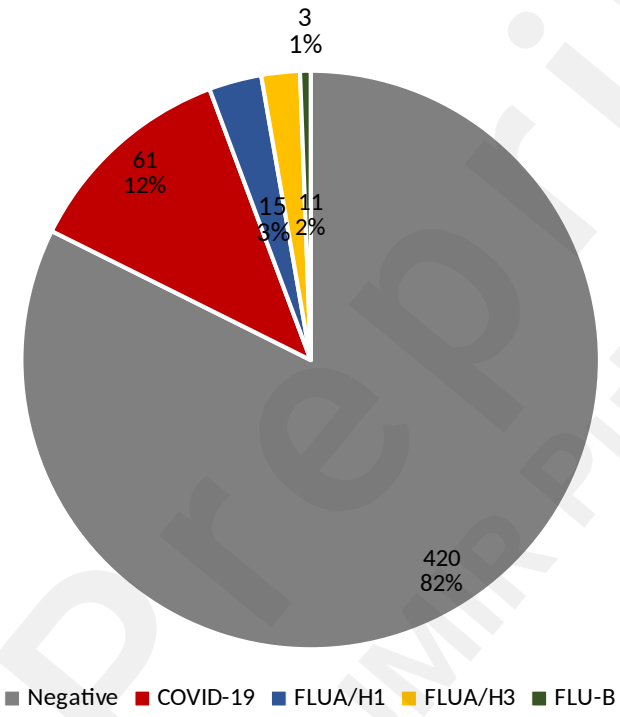
Most of the cases with co-infection reported had predisposing factors reducing their immunity and many of them required mechanical ventilation and/or ICU admission [6-9,13]. It was found that more than 60% of patients with co-infection had comorbidities, 33% needed artificial ventilation, and 29% were admitted to ICU5. Up-to date the case reported from Egypt is the only one with mild upper respiratory symptoms reported from any country. This could be related to her age and gender in addition to the absence of pre-disposing comorbidities.

Results of ILI patients testing indicated that more than 80% of cases were negative for both SARS-CoV-2 and influenza. Broader viral testing might be needed to identify the etiology particularly if it would affect patient treatment [13].

Conclusion:

Egypt is reporting a case of SARS-CoV-2 and influenza A/H1 co-infection with mild ILI symptoms. This finding suggested that co-infection can occur in people of younger ages with no comorbidities. The report showed that patient immunity can overcome both infections leading to full recovery in a short period with no need to medical procedures. ILI surveillance proved effective in detection of the viral causes of patients with ILI symptoms. Broadening of the testing panel is recommended especially if it could guide improve case management guidelines.

Figure 1. viral causes of 510 specimens collected from influenza like illness (ILI) sentinel surveillance, Egypt, October 2019-September 2020.



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Supplementary Files

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Figures

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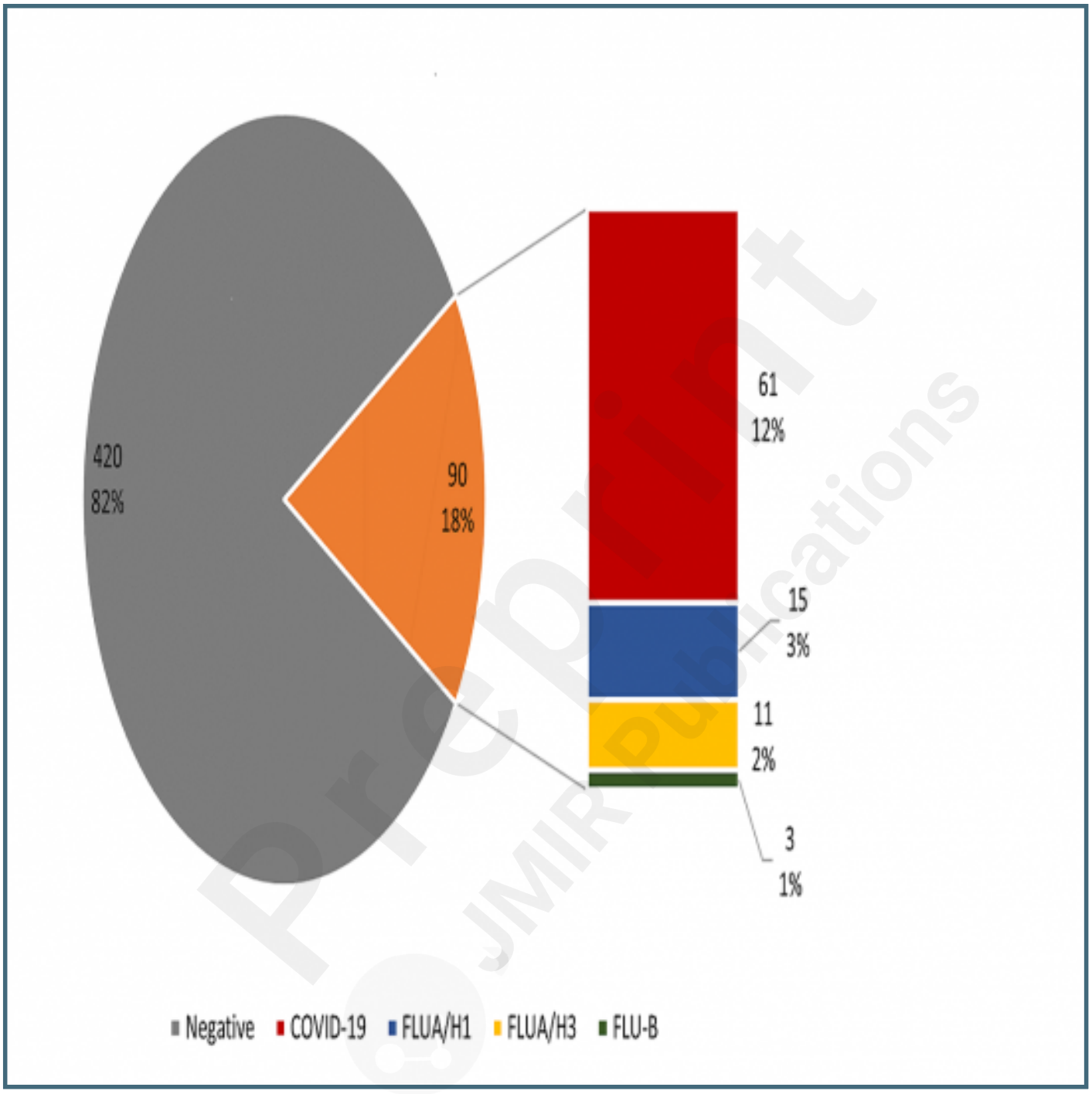
420
82%
90
18%
61
12%
15
3%
11
2%
3
1%
Negative
COVID-19
FLUA/H1
FLUA/H3
FLU-B