

Original Article

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Experience from a COVID-19 first-line referral clinic in Greater Copenhagen

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ABSTRACT

INTRODUCTION: Due to the coronavirus disease 2019 (COVID-19) exposure in Denmark, first-line referral centres were established to handle all patients suspected of COVID-19 or other upper respiratory tract infection. Here we report the first experiences from a first-line referral centre from Amager-Hvidovre Hospital, situated on the outskirts of Copenhagen.

METHODS: A retrospective quality assessment was performed with collection of symptom patterns and COVID-19 status.

RESULTS: During the first 24 days, a total of 3,551 patients were referred for assessment of symptoms of upper respiratory tract infection and COVID-19. A total of 2,048 patients were assessed as having mild symptoms and referred for COVID-19 testing alone, whereas 337 patients were assessed clinically by a physician. Thirty-seven were positive for COVID-19 infection, 286 were negative. The most common symptoms reported were fever, coughing and dyspnoea. Fever was an independent predictor of COVID-19 infection (odds ratio (OR) = 2.25 (95% confidence interval (CI): 1.08-5.04); $p = 0.037$); whereas sore throat was not (OR = 0.40 (95% CI: 0.15-0.92); $p = 0.045$). Only a small number of patients reported loss of taste or anosmia. In total, 113 patients were admitted to hospital, the majority of patients were discharged within 24 hours with mild symptoms of upper respiratory tract infections. Three of the COVID-19-positive patients developed a severe infection and two had a fatal outcome.

CONCLUSIONS: The present study is the first to report the experiences and symptom patterns of a COVID-19 first-line referral centre with efficient triage of patients in need of hospitalisation.

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing the coronavirus disease 2019 (COVID-19), has evolved into a pandemic within the past five months, with more than eight million verified cases worldwide [1, 2]. It is a viral infection with similarities to the 2003 severe acute respiratory syndrome (SARS). Most patients experience mild to moderate symptoms [1]. However, a minority of patients develop severe respiratory distress syndrome, but the numbers reported vary from 4% to above 20% [3-5]. The natural course of the infection is characterised by an incubation period of up to 18 days and a minimum disease duration of 14 days, with risk of progression even late in the disease course [6-8].

The viral load is highest in the first week of infection, and seroconversion is present in all patients after 14 days [9].

The symptoms mimic those of other upper respiratory tract infections, with fever and coughing as the most commonly reported symptoms. In total, 25-88% of patients report fever and 28-46% report coughing [3, 10, 11]. Other symptoms reported are headache, muscular pain and sore throat. Furthermore, cases of anosmia and taste dysfunction have been reported [12, 13].

The clinical handling of patients depends on the infrastructure of medical healthcare in the respective countries [14, 15].

In Denmark, a first-line referral centre (COVID-19 clinics) for handling of patients with symptoms of upper respiratory tract infection was set up from 16 March 2020 as part of Danish COVID-19 health care management [16]. COVID-19 clinics were established in emergency hospitals in order to introduce an additional selective filter between primary care and hospitals to prevent unnecessary resource use and the overfilling of hospitals, which was a considerable challenge in other European countries.

The primary tool in testing for COVID-19 is the nasopharyngeal swab [8, 9]. In Denmark, COVID-19 testing was initially offered to people with suspected COVID-19 infection, such as tourists returning from endemic areas. As the virus became more widely spread, the testing strategy was widened to include patients with moderate to severe symptoms of upper respiratory tract infection. As of 28 March 2020, testing was made available to all persons with symptoms and a high risk of infection such as social workers and healthcare workers, patients with co-morbidities and patients with mild symptoms [16].

In this study, we aimed to evaluate the symptom pattern of COVID-19 and the overlap with other upper respiratory tract infections in patients referred for first-line evaluation at a Danish COVID-19 clinic in Hvidovre in the greater Copenhagen area.

METHODS

Our COVID-19 clinic was established on 16 March 2020 as part of the emergency facilities for management of the COVID-19 epidemic in Denmark. Organisationally, the clinic is managed by the Gastro Unit, Amager-Hvidovre Hospital, and staffed with personnel from several medical and surgical specialties. Senior physicians specialising in internal medicine are always present during opening hours (8 AM-10 PM).

The COVID-19 clinic is a first-line referral centre, assessing patients with symptoms of upper respiratory tract infections who are under suspicion for COVID-19. Due to safety procedures implemented to avoid further community spread of the infection, these persons were unable to be clinically assessed in general practice. General practitioners and the emergency medical services (emergency telephone 112, and medical helpline 1813) referred patients for both clinical evaluation and testing for COVID-19 by throat swab who would in many cases otherwise have been admitted directly to a COVID-19 medical ward [17]. All patients were initially interviewed by telephone.

On 26 March 2020, the Danish health authorities expanded their testing strategy. After this date, all patients assessed clinically in the COVID-19 clinic were also tested for COVID-19.

In the COVID-19 clinic, patients underwent a physical examination including pulmonary and cardiac auscultation, measurement of rectal temperature, blood pressure, heart rate, respiratory rate and oxygen saturation. If relevant, a quick-test C-reactive protein (CRP) by finger prick was performed. If the patient needed further diagnostic investigations such as a chest x-ray or laboratory testing, relevant referral or admission to a COVID-19 acute hospital ward was ensured. Admission or treatment via the COVID-19 clinic for other causes than COVID-19 was registered.

All patients were interviewed about symptoms of respiratory tract infection, duration of symptoms, co-morbidities and risk of COVID-19 infection or exposure. A follow-up of the hospitalised patients was performed on 11 May 2020. Furthermore, two weeks after evaluation in the COVID-19 clinic, the regional medical files for all patients who were not hospitalised were checked for subsequent admittance.

The present retrospective study was performed as part of an internal quality assessment and approved by the Hospital Directory Board on 12 April 2020.

Statistical analysis

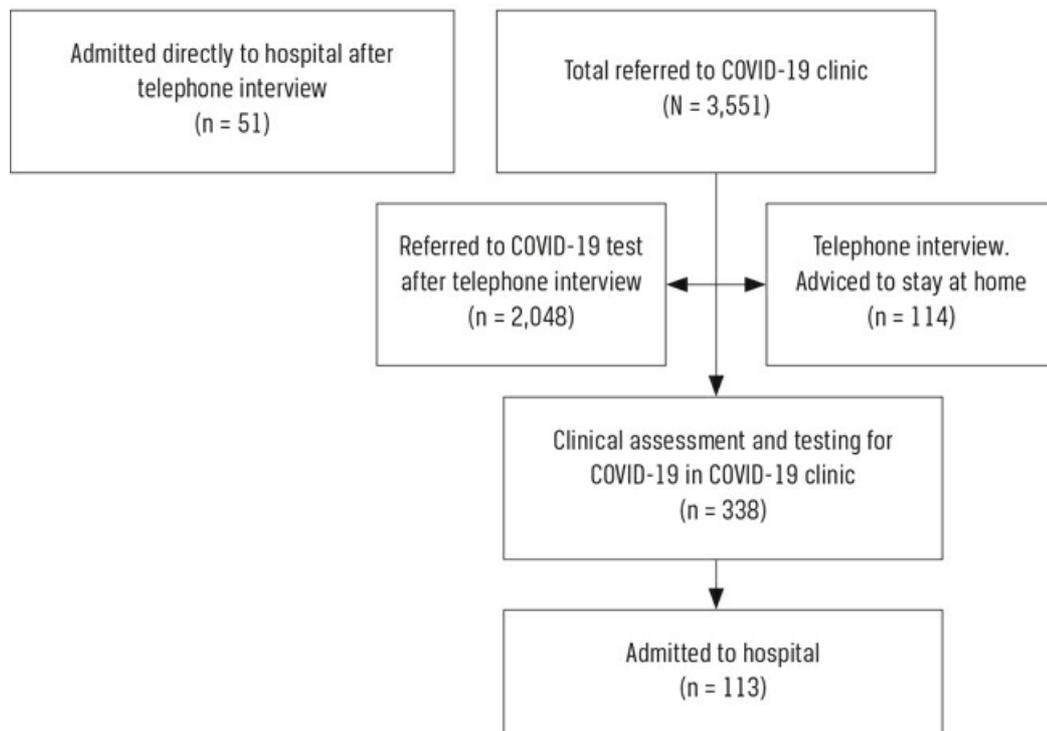
We analysed data using GraphPad Prism 8.02 and R version 3.6.0. Based on the distribution of data, patient characteristics were reported as median and range. Comparison between groups was conducted using non-parametric t-testing (Mann-Whitney), and comparison of the probability of symptoms was done by logistic regression. Results are stated as odds ratio and 95% confidence interval.

Trial registration: not relevant.

RESULTS

In the period from 16 March to 8 April 2020, 3,551 patients were referred to the COVID-19 clinic. A patient flow chart of patients referred to the COVID-19 clinic is presented in Figure 1.

FIGURE 1 / Patient flow chart of patients referred to the coronavirus disease 2019 (COVID-19) clinic between 15 March and 8 April 2020.



Among these, 1,114 were given general advice (stay at home until complete restitution, perform self-isolation until 48 hours after resolution and use over-the-counter drugs such as paracetamol) and they were instructed to contact a doctor again if dyspnoea or aggravation of symptoms occurred. Another 2,048 were assessed by telephone interview to have mild symptoms with no need to see a physician, but it was assessed that testing for COVID-19 virus was relevant. These patients were referred directly for testing by throat swab in the outpatient test clinic. These patients were also strictly informed to perform self-isolation until 48 hours after complete remission. A total of 48 persons were admitted directly to a dedicated COVID-19 emergency ward after their telephone interview. Furthermore, 338 persons were estimated to be in need of primary clinical assessment. Among these, 113 persons admitted to hospital following further assessment.

Among the 338 patients, 37 had a positive COVID-19 test, either by throat swab or by real-time reverse transcription polymerase chain reaction (RT-PCR) of tracheal secretion. The tracheal secretion test was only performed during admission to hospital and not in the

COVID-19 clinic. Fourteen persons were not tested for COVID-19, which limited our possibility of characterising differences between positive and negative COVID-19 patients. One person who was COVID-19 positive was assessed and tested twice. This person was only characterised as one patient, which reduces the number of total patients to 323 (338 – 14 – 1 = 323). The remaining 286 patients were COVID-19 negative. Among all assessed patients, 125 were males (38.5%), and their age ranged from 18 to 89 years, see **Table 1**.

TABLE 1 / Patient characteristics of admitted patients in the coronavirus disease 2019 (COVID-19) clinic, tested for COVID-19.

	COVID-19 status		p-value ^a
	Positive (n = 37)	Negative (n = 286)	
Age, median (range), yrs	51 (30-85)	49 (18-89)	0.25
Gender, male, n (%)	13 (35.1)	112 (39.2)	-
<i>Blood pressure, median (range), mmHg</i>			
Systolic	133 (102-166)	134 (101-197)	0.54
Diastolic	84 (61-111)	85 (36-130)	0.41
Heart rate, median (range), beats/min.	86 (60-128)	84 (49-140)	0.69
Respiratory rate, median (range), inspirations/min.	21 (12-40)	20 (10-32)	0.25
O ₂ saturation, median (range), %	97 (89-100)	97 (81-100)	0.62
Rectal temperature, median (range), °C	37.8 (36.0-40.3)	37.4 (34.5-40.0)	0.002
Travelling history < 8 wks, n (%)	3 (8.1)	33 (11.5)	-
Reported co-morbidities, n (%)	17 (46,0)	157 (54,9)	-
Symptom duration, median (range), days	9 (2-21)	7 (1-75)	-

a) Analysed by Mann-Whitney non-parametric t-test. Nominal values were analysed with χ^2 -test.

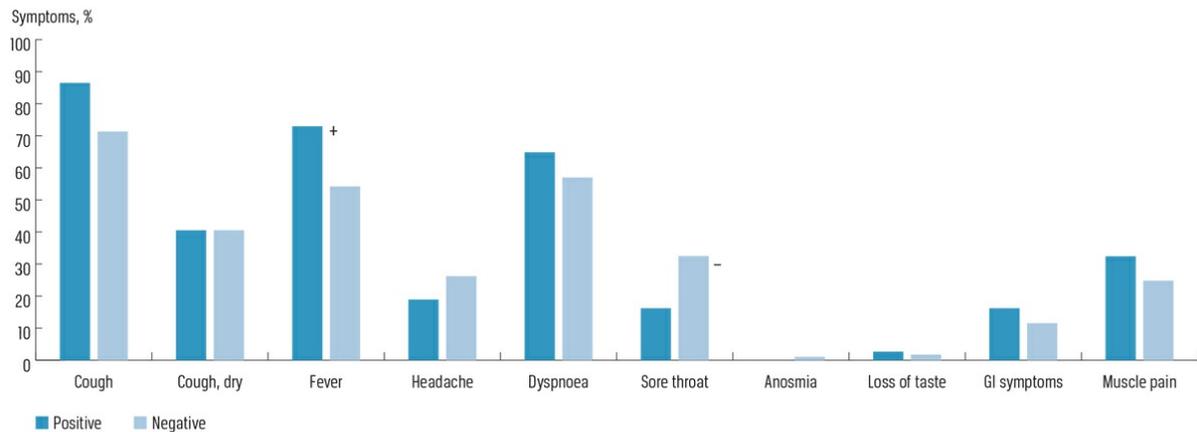
Five of the 37 COVID-19-positive patients had repeated tests. Three were confirmed positive by repeated throat swab, two were confirmed positive by PCR of tracheal secretion and two patients had a negative throat swab, but COVID-19 infection was confirmed by tracheal secretion. Twenty of the 286 patients who were COVID-19 negative had repeated testing. Thirteen patients had repeated throat swab, all were negative; and seven patients had PCR of tracheal secretion, all repeated test results were negative.

The main features characterising the patients in need of admission to hospital was dyspnoea, low oxygen saturation or high temperature, or suspected bacterial infection requiring intravenous antibiotic treatment.

A total of 177 patients reported co-morbidities (5.8%). The most frequent co-morbidities were pulmonary diseases (asthma, chronic obstructive pulmonary disease, or both), eight of 38 (21.1%) patients in the COVID-19 positive group, and 78 of 285 patients (27.4%) in the COVID-19 negative group; and cardiovascular disease, seven of 38 (18.4 %) in the COVID-19 positive group and 32 of 285 (11.2%) in the COVID-19 negative group, respectively.

A variety of symptoms were reported (**Figure 2**). The most frequent were fever and coughing, both dry and productive. By logistic regression, we found fever to be a predictor of COVID-19 infection (**Table 2**), cough tended towards prediction of COVID-19, whereas muscle pain and headache did not. Anosmia and loss of taste were reported in very few cases. Having a sore throat was a negative predictor of COVID-19 infection.

FIGURE 2 / Comparison of self-reported symptoms between coronavirus disease 2019 (COVID-19)-positive and COVID-19-negative patients*.



GI = gastrointestinal.

a) Fever was a positive predictor of COVID-19 infection (odds ratio (OR) = 2.21 (95% confidence interval (CI): 1.08-5.04); $p = 0.037$) indicated by a +, whereas sore throat was a negative predictor of COVID-19 infection (OR = 0.40 (95% CI: 0.15-0.92); $p = 0.045$) indicated by a -.

TABLE 2 / Comparison of frequency of reported symptoms in patients positive vs negative for coronavirus disease 2019.

	OR (95% CI)	p-value
Cough	2.53 (0.95-6.72)	0.063
Fever	2.21 (1.08-5.04)	0.037
Dyspnoea	1.37 (0.68-2.88)	0.38
Sore throat	0.40 (0.15-0.92)	0.045
Gastrointestinal symptoms: nausea, vomiting or diarrhoea	1.44 (0.51-3.48)	0.45
Muscle pain	1.49 (0.69-3.07)	0.30
Headache	0.64 (0.25-1.45)	0.32
Anosmia	-	-
Taste	1.56 (0.08-10.0)	0.69

CI = confidence interval; OR = odds ratio.

From the COVID-19 clinic, 113 patients were admitted to hospital. A total of 91 were discharged within 24 hours; none of these had severe COVID-19 infection. Furthermore, 26 were treated for other diseases, primarily bacterial infections, 22 had COVID-19 infection. Two had a fatal outcome, 110 were discharged and one patient is still (as of 11 May 2020) hospitalised in an intensive care unit.

Of the fourteen patients who were not tested for COVID-19, nine were admitted to the acute

medical ward for investigations for other infectious diseases (all prior to 26 March 2020 when only patients with moderate to severe symptoms were offered COVID-19 testing), four had obvious clinical signs other disease than COVID-19 and one left the ward prior to testing.

Six patients were re-evaluated within one week, either in the COVID-19 clinic or the acute medical ward. One patient was admitted to hospital 24 hours after clinical assessment in the COVID-19 clinic with a marked progression in clinical symptoms.

DISCUSSION

A total of 323 patients were assessed in the COVID-19 clinic from 16 March to 8 April 2020. Compared to those advised by telephone only, the patients assessed were evaluated initially by anamneses and by respiration on the telephone. Clinical suspicion of severe disease or in circumstances such as language barriers, anxiety or patients whose symptoms generated doubts were referred to the COVID-19 clinic for further assessment. Many patients were dismissed after clinical assessment in the COVID-19 clinic, and the number of patients in need of hospitalisation was very low. Many patients admitted were dismissed shortly after assessment, further confirming that most patients with symptoms of COVID-19 or other airway virus disease were able to handle their symptoms and disease at home.

Thirty-seven of the assessed patients were positive for COVID-19 infection. Dyspnoea, fever, sore throat and gastrointestinal symptoms were predictors of COVID-19 infection, whereas cough, muscle pain and headache were not.

The patients were relatively young and more often female, which is in line with other cohorts reported from Europe [18]. All patients were handled after new, but consistent triage guidelines of clinical assessment, and data were collected consecutively in a quality assessment database. However, the lack of a protocolled study design limited follow-up of patients.

A study of the characteristics and predictors of patients with a positive RT-PCR test in Denmark between 27 February and 30 April revealed only minor differences in age, sex, medical history and prior drug use between positive and negative test cases [19]. This is similar to our findings. However, there is a discrepancy between patients admitted to hospital from the clinic (59.4%, **Supplementary Table S1**) and the fraction of patients with positive SARS-CoV-2 (22%) hospitalised in total. Patients referred from the COVID-19 clinic were assessed clinically and were more likely to be in demand of hospital care than the total number including symptom-free persons who had tested positive.

Testing in the COVID-19 clinic was performed with QIAstat-Dx Respiratory-nCoV Panel Assay, which is a commercially available kit with a limit of detection of > 95% [20]. Two patients had a negative throat swab but were confirmed positive by tracheal secretion. We believe that testing sensitivity is strongly influenced by the timing of testing and symptom pattern. This

may explain the difference in results. Test sensitivity and specificity also depend on testing methods, the frequency of other infections in the community and the lack of a gold standard for SARS-CoV-2 virus. Only hospital departments had the possibility to perform the tracheal secretion analysis. In the COVID-19 clinic, the purpose was not to diagnose or treat serious cases of COVID-19 – they were referred immediately to other relevant instances. The costs and practicalities of making tracheal suction were deemed too intricate for the COVID-19 clinic given the patient type assessed here.

A quick test CRP analysis was established in the clinic as the profits were clear shortly after opening. This mimics the possibilities in the primary sector in Copenhagen that the clinic was established to relieve. If further biochemical analyses were necessary, patients were referred to a hospital department.

The duration of symptoms varied markedly for both positive and negative COVID-19 patients. The number of days was rarely exact when patients were reporting, and the design of this study limits further conclusions as to the general symptom duration of COVID-19.

The gatekeeper function intended by establishing the COVID-19 clinic was shown to be highly effective; only 337 of the 3,551 persons referred were assessed in the clinic. In the beginning of the epidemic, the throat swab was only provided for patients who were highly suspect for COVID-19; hence, 14 individuals did not receive the swab even though they were referred to hospital. Only one person experienced marked progression in symptoms after the evaluation in the clinic and reacted sufficiently hereupon.

Our data do not reflect the destiny of the patients only assessed by telephone interview. However, every patient assessed clinically was checked for multiple contacts. This number was very low, and we assume that the risk of underestimating the gravity of patients' symptoms is low, although this setup is unsuited for a conclusion in this respect. The doctors in the COVID-19 clinic had a suitable basis for professional assessments as their level of education was determined to be above basic clinical training and at least one senior doctor was on duty in the clinic at all times.

CONCLUSIONS

In conclusion, specific symptoms of fever and dyspnoea were more often seen in patients with COVID-19 infection, whereas a sore throat was a negative predictor. The COVID-19 clinic served as a first-line referral centre from general practitioners and emergency medical services with effective triage of patients, and also held a gatekeeper function for direct admission to acute medical wards.

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