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B.1.1.7 Variant Outbreak in an Air Force Military Base—Real-World Data

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ABSTRACT

Objective:

To assess the clinical features and infectivity of variant B.1.1.7 among healthy young adults in a military setting.

Materials and Methods:

Positive cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a single military base (March 23, 2020 and February 16, 2021) were included. An epidemiological investigation conducted via phone included questions regarding symptoms, exposure history, smoking status, list of contacts, and recently visited places. Symptoms surveyed included fever, cough, shortness of breath, sore throat, loss of smell or taste, gastrointestinal symptoms (GI), headache, chest pain, and constitutional symptoms. Cases were divided before B.1.1.7 first reported case in Israel (December 23, 2020) (period 1) and after its identification (period 2). Symptom distribution and the risk of a contact to be infected were compared between the periods, using a chi-square test, and a negative binominal regression model, respectively.

Results:

Of 293 confirmed cases, 89 were reported in the first period and 204 in the second. 56.0% were men with a median age of 19.5 years (interquartile range 18.6-20.5). GI symptoms, loss of taste or smell, headache, fever, and chills were more prevalent in the first period ($P < .001$, $P = .026$, $P = .034$, $P = .001$, and $P < .001$, respectively), while fatigue was more common in the second period ($P = .008$). The risk of a contact to be infected was three times higher in the second period (relative risk $= 3.562$ [2.414-5.258]).

Conclusion:

An outbreak of SARS-CoV-2 in young healthy adults, during a period with high national-wide B.1.1.7 variant prevalence, is characterized by decreased prevalence of fever, loss of taste or smell and GI symptoms, increased reports of fatigue, and more infected contacts for each index case.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in China on December 2019[1] and was shortly declared as a pandemic.[2] As of September 2021, the reported disease burden exceeds 220 million people, with a death toll of approximately 4,600,000 worldwide.[3] In the past year of the pandemic, mounting evidence has been published regarding Coronavirus disease 2019 (COVID-19) presentation and risk factors for severe disease and mortality,[4–7] while the population of young adults has not been studied extensively.[6,8,9] On December 14, 2020, the World Health Organization announced the identification of a variant of concern, first reported in the United Kingdom.[10,11] This variant, later known as B.1.1.7, contained several mutations, some of which involved the receptor-binding domain, leading to higher disease transmissibility.[12–14] Since its identification, B.1.1.7 propagated in an unprecedented pace, quickly spread to more than 93 countries,[15] and became the dominant variant in many countries worldwide.[14,16,17] In Israel, the first case of B.1.1.7 was reported on December 23, 2020, and by February, the variant was isolated in over 90% of all newly identified cases.[18] Along with higher transmissibility, observational studies suggested higher rates of infection and hospitalization in young adults.[19-21] However, sparse data are available regarding the effects of the B.1.1.7 on disease presentation, symptomatology, severity, and age distribution. Available data are driven primarily from ecological and survey studies with conflicting results.[22,23] While some report no difference in presenting symptoms,[22] others report a higher rate of fever, cough, and shortness of breath (SOB) with B.1.1.7. As SARS-CoV-2 continues to mutate quickly, leading to ever-changing variants of concern, a better understanding of phenotypic variance that arise from the genetic changes of previous variants can serve the health community in efforts to predict the clinical expression of current and future ones. In this retrospective

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cohort study, we used a recent outbreak of the B.1.1.7 variant in an Israel Defense Force (IDF) military base to compare the clinical characteristics of B.1.1.7 infection with previous outbreaks in healthy young adults.

METHODS

Study Population

We included all positive cases of SARS-CoV-2 in a single Air Force military base identified between March 23, 2020 and February 16, 2021. A confirmed case was defined according to the Israeli Ministry of Health guidelines by having a positive real-time reverse transcription polymerase chain reaction (rRT-PCR) test for SARS-CoV-2. Eligibility for confirmatory testing was directed by the surgeon general and approved by certified public health officers on a case-by-case basis. The testing policy directive evolved with time, according to international and national guidelines to include the presence of symptoms (cough, SOB, sore throat, fever >38°C, and loss of taste or smell) and/or a suspicious exposure (including a SARS-CoV-2 positive household contact). A detailed list with testing criteria by time is available in Supplementary material (p. 5).

Data Collection

The epidemiological division of the IDF medical corps handled the documentation of all individuals with suspicious symptoms, those in need for quarantine, and all confirmed COVID-19 cases. This included collection of data obtained through contact tracing and epidemiological investigations of each positive case. The epidemiological survey was conducted via phone and included questions regarding symptoms and date of onset, exposure history (i.e., contact with a confirmed case), past medical history, smoking status, list of contacts and recently visited places, and means of transportation. Symptoms surveyed during epidemiological investigation included fever >38°C, cough, SOB, sore throat, loss of smell or taste, gastrointestinal (GI) symptoms (i.e., abdominal pain and/or diarrhea), headache, chest pain, and constitutional symptoms such as fatigue, chills, and myalgia. This thorough inquiry was performed shortly after disease confirmation and no longer than 24 hours after a positive PCR test result. In order to distinguish presymptomatic from asymptomatic patients, isolation admission and discharge summaries of all asymptomatic patients were reviewed for symptoms that developed during the isolation period. All information was recorded in a computerized database. The following covariates were abstracted from the medical registry: body mass index (BMI), baseline health status and comorbidities, rank, and position, as previously reported[24–26] and detailed in the Supplementary extended methods.

Viral RNA Test

The presence of viral RNA was examined using rRT-PCR based on the SARS-CoV-2 Centers for Disease Control and Prevention protocol.[27] Cycle threshold values, as well as internal control, were reported for each of the three viral genes (RdRP, N gene, and E gene). A threshold of 40 cycles or below was considered positive. Additional details on testing methods are available in previous reports.[28] All tests were performed by a Ministry of Health authorized laboratory.

In the case of retesting positive for SARS-CoV-2, the cycle thresholds were compared to the previous result, epidemiological and clinical information was gathered, and a serological blood test for SARS-CoV-2 IgM and IgG was taken. The epidemiological division of the IDF used the combined information to decide whether this case was a reinfection or a false-positive result.

Statistical Analysis

The prevalence of reported symptoms and exposure was compared between two periods, as shown in Figure 1, before the identification of the B.1.1.7 variant in Israel (i.e., March 23-December 23) and after the first reported B.1.1.7 case (i.e., December 24-February 16). Continuous variables were presented as medians and interquartile ranges (IQRs), and categorical variables were presented as percentages and counts. A univariate analysis assessed the association between the study period and demographic (age and sex), clinical (baseline health status, BMI, and various comorbidities), smoking, and service characteristics (mandatory/professional, rank) using a chi-square test. This test was also used to compare the symptom prevalence between periods. A further analysis aiming to assess the difference in infected contacts between periods included only participants who reported on epidemiological contacts in the base ($n = 236$). A univariate negative binomial regression model with number of SARS-CoV-2 positive cases among the contacts of each index patient as a dependent variable and with natural logarithm (LN) of number of contacts as a covariate (offset variable) was used to assess the risk for infecting others between study periods. Further, a multivariate negative binomial regression model was used, with additional variables (age, sex, type of service, baseline health status, presence of symptoms, number of symptoms, and presence of a specific symptom) along with the study period. Relative risk (RR) was considered statistically significant if two-sided P-value was <.05.

Statistical analyses were conducted using Microsoft Excel (version 2013) and IBM SPSS for Windows (version 25.0).

The institutional review board of the IDF approved this study (protocol number 2092-2020) and waived the requirement for written informed consent based on preserving participants' anonymity.

RESULTS

Overall, 293 positive cases of SARS-CoV-2 were identified in a single Air Force base, between March 23, 2020 and February 16, 2021, of which 89 were identified during the first study period and the remaining 204 were identified during the second study period (Fig. 1). Over half were men ($n = 164$,

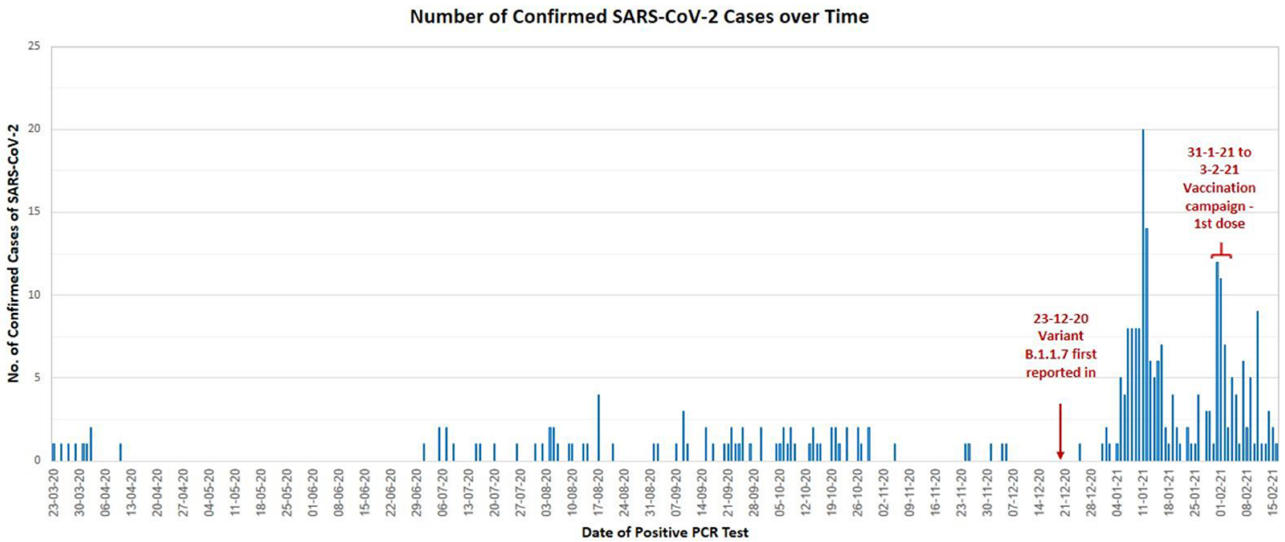

FIGURE 1. Number of confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cases over time. On December 23, 2020, the first case of variant B.1.1.7 was reported in Israel. Study groups were selected accordingly, before and after this date. Until December 23, 89 cases were accumulated in a period of approximately 10 months. After December 23, 204 cases accumulate rapidly during 2 months only. A military vaccination campaign at the base took place between December 31 and February 3, 2021. In this period of time, cumulatively 50.0% of the base population were vaccinated with the first dose of the Pfizer BNT162b2 vaccine. Please see Supplementary Table S1 in the supplement for elaboration.

TABLE I. Baseline Characteristics of Study Population Comparing Two Periods: Before B.1.1.7 First Reported Case in Israel (Period 1) and After Its Identification (Period 2)

	Overall ($n=293$)	Period 1 (March 23-December 23) (n, % of overall) ($n=89$)	Period 2 (December 24-February 16) (n, % of overall) ($n=204$)	P-value
Age (years); median (IQR)	19.5 (18.6–20.5)	20 (19–22)	19 (18.5–20)	<0.001
Male sex, n (%)	164 (56.0)	52 (58.4)	112 (53.8)	0.576
Type of service, n (%)				
Mandatory	253 (86.3)	66 (74.2)	187 (91.7)	<0.001
Rank, n (%)				
Private[a]	157 (53.6)	18 (20.2)	139 (68.1)	<0.001
Unimpaired health[b], n (%)	169 (58.3)	52 (59.1)	117 (57.9)	0.864
Asthma[c], n (%)	23 (7.9)	7 (8.0)	16 (7.9)	0.995
Allergic rhinitis, n (%)	21 (7.2)	3 (3.4)	19 (9.4)	0.093
Chronic sinusitis, n (%)	0 (0)	0 (0)	0 (0)	–
Hypertension, n (%)	2 (0.7)	0 (0)	2 (1.0)	1.000
Smoking, n (%)	41 (14.3)	16 (19.3)	25 (12.3)	0.194
Body mass index (BMI), n (%)				
BMI < 18.5	15 (5.2)	7 (8.0)	8 (4.0)	0.162
BMI 18.5-24.9	170 (59.0)	45 (51.1)	125 (62.2)	0.087
BMI 25-29.9	64 (22.2)	18 (20.5)	46 (22.8)	0.658
BMI $\geq$ 30	39 (13.5)	17 (19.3)	22 (10.9)	0.054

$P < .05$ is considered statistically significant.
[a]Private, i.e., new enlisted trainee.
[b]Definition and method for the determination of unimpaired health is detailed in Supplementary material.
[c]History of childhood asthma, with no use of inhaler for 3 or more years, and normal pulmonary function tests do not affect medical fitness.

56.0%), with a median age of 19.5 (IQR 18.6-20.5) years. More than 85% ($n=253$) of cases occurred in individuals in mandatory military service, who usually spend extended periods in base (compared with professional army personnel), with 53.6% ($n=153$) of SARS-CoV-2 infections seen in newly enlisted trainees. The characteristics of the study population are shown in Table I.

Reported Symptoms and Epidemiological Exposure

Contact with a confirmed SARS-CoV-2 case was reported in 75.3% ($n=67$) and 77.5% ($n=158$) of cases in the first and second periods, respectively. During the first period, the place of presumed infection was traced in above 75% ($n=69$) of cases and was evenly distributed between inside (50.7%, $n=35$) and outside (49.3%, $n=34$) the confines of the base.

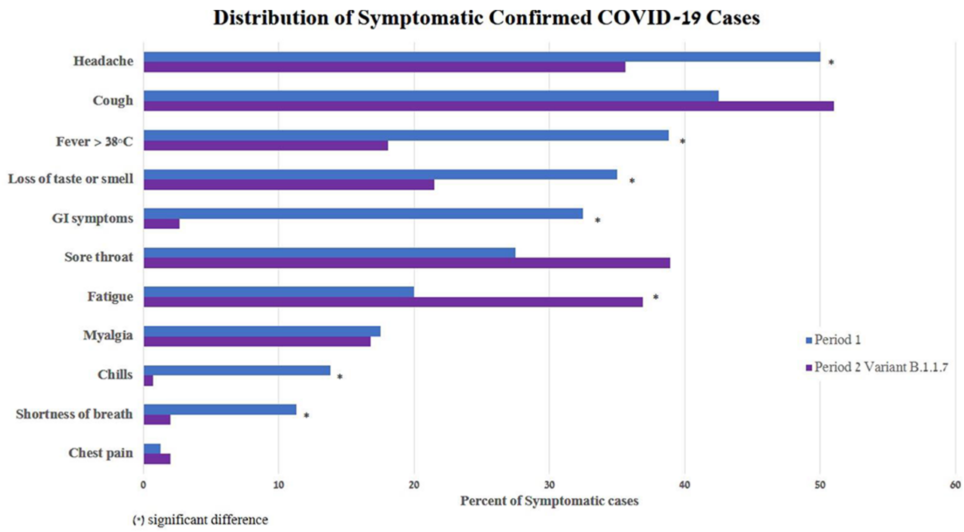

FIGURE 2. Distribution of symptomatic cases of Coronavirus disease 2019 (COVID-19) over time. Period 1 (blue), March 23-December 23, represents cases before the identification of variant B.1.1.7 is Israel. Period 2 (purple), December 24-February 16, represents cases attributed to the variant B.1.1.7. During the second period, B.1.1.7 was the dominant variant in Israel and also genotyped from two cases (out of two) from a large infection cluster at the time. *Significant difference between groups.

In the later period, more infections were traced to the base (76.6%, $n = 121$, $P = .002$) than outside the base (23.4%, $n = 37$, $P < .001$). The reinfection rate was 0% ($n = 0$) in both periods. 89.8% ($n = 80$) of cases in the first period were symptomatic, of which the most commonly reported symptom was headache (50.0%, $n = 40$), followed by cough (42.5%, $n = 34$) and fever (38.8%, $n = 31$) (Fig. 2). During the second period, symptoms were reported in only 73.0% ($n = 149$) of infected individuals ($P = .001$). The most commonly reported symptom was cough (51.0, $n = 76$), followed by sore throat (38.9%, $n = 58$) and fatigue (36.9%, $n = 55$). GI symptoms, loss of taste or smell, headache, fever, and chills were all more prevalent in the first period compared with the second ($P < .001$, $P = .026$, $P = .034$, $P = .001$, and $P < .001$, respectively). The opposite trend was seen with fatigue, which was more common in the later period (36.9%, $n = 55$) compared with the first (20.0%, $n = 16$) ($P = .008$).

Infected Epidemiological Contacts

As shown in Figure 1, the epidemic curve growth in base increased dramatically in the second period of the study. Until December 23, 2020, 89 cases accumulated over a period of 10 months, and after this date more than twice the number of cases (204) accumulated over a period of 2 months.

During the first period, each confirmed case reported on average of 10 (range 0-73) close contacts inside the unit, of which an average of 1.3 (range 0-6) contacts (10.41% [0-62.5%]) were ultimately identified as confirmed SARS-CoV-2 cases. In the second period, a higher proportion of infected contact was seen. Each confirmed case reported an average of 5 (0-23) close contacts inside the unit, of which 2.3 (0-12) (41.60% [0-100%]) were ultimately identified as confirmed cases.

Using a univariate negative binominal linear regression model (Table II, Supplementary Table S2), the risk of a contact to be infected was found to be three times higher in the second period compared to the first (RR = 3.562 [2.414-5.258]). In addition, type of service (mandatory vs. professional) was also significantly associated with a higher risk of a contact to be infected (RR = 1.869 [1.065-3.278]). However, the study period was the only factor independently associated with a higher risk of infection in a multivariate analysis.

There were no major differences in public health measures and restrictions used in order to mitigate disease propagation between the two study periods (p. 4, Supplement material).

DISCUSSION

Sparse data were published regarding the SARS-CoV-2 variant B.1.1.7, which propagated rapidly and became the dominant variant in many countries worldwide including Israel. In this study, we report the clinical characteristics of an outbreak of SARS-CoV-2 occurring during a period with a very high national prevalence of variant B.1.1.7 in young healthy adults in a military setting. We report a higher proportion of fatigue and lower proportion of GI symptoms, loss of taste or smell and fever, and a risk three times higher for a contact of an index case to be infected with the virus during this period.

Variant B.1.1.7 was first reported in September 2020 in the United Kingdom.[10] This variant carries a constellation of genetic mutations, including in the S protein receptor-binding domain, which is essential for binding to the host cell angiotensin-converting-enzyme-2 receptor, which facilitates virus entry into cells.[16] Multiple lines of evidence indicate that

TABLE II. Risk of Infecting Others, Results of the Unadjusted and Adjusted Multivariate Negative Binominal Regression Model

Soldier's characteristics		Unadjusted Relative Risk (RR) [CI 95%]	Adjusted RR[a] [CI 95%]	
Period	Period 1 vs. period 2	3.562 [2.414–5.258]	Period 1 vs. period 2	soldier characteristics
Age	≤19.5 years (median) vs. 19.6 years and older	1.337 [0.964–1.855]	3.700 [2.431–5.632]	0.918 [0.644–1.308]
Gender	Female vs. male	1.105 [0.796–1.534]	3.673 [2.463–5.479]	1.105 [0.796–1.534]
Body mass index (BMI)	25–29.9 vs. ≤24.9	1.279 [0.842–1.941]	3.532 [2.382–5.237]	1.061 [0.693–1.623]
	30+ vs. ≤24.9	1.252 [0.759–2.066]		1.049 [0.634–1.736]
Smoking	yes vs. no	0.694 [0.416–1.157]	3.328 [2.243–4.936]	0.694 [0.416–1.157]
Baseline health	Unimpaired[b] vs. impaired health	0.902 [0.649–1.252]	3.556 [2.409–5.249]	0.923 [0.664–1.283]
Rank	Private[c] yes vs. no	1.076 [0.709–1.633]	3.386 [2.086–5.498]	1.076 [0.709–1.633]
Type of service	Mandatory vs. professional	1.869 [1.065–3.278]	3.425 [2.304–5.091]	1.337 [0.767–2.333]
Symptom existence	Symptomatic vs. asymptomatic	0.777 [0.529–1.142]	3.531 [2.388–5.221]	0.849 [0.580–1.243]

This table summarizes the results of the unadjusted (univariate) and adjusted (multivariate) binominal linear regression model. RR with 95% confidence interval exclusive of the null is considered statistically significant (bold). Period 1: before the identification of B.1.1.7 variant in Israel (i.e., March 23-December 23); period 2: after the first reported B.1.1.7 case (i.e., December 24-February 16). Results show that the period and type of service were the only factors associated with the risk of a contact to be infected in the unadjusted univariate model, while only the former was independently associated with infection in a multivariable analysis.

[a]The multivariable model includes period with each of the soldier's characteristics at a time.

[b]Definition and method for the determination of unimpaired health is detailed in supplementary material.

[c]Private, i.e., new enlisted trainee.

B.1.1.7 is more efficiently transmitted compared with other SARS-CoV-2 variants. Geographic regions with a higher proportion of B.1.1.7 sequences had faster epidemic growth than did other areas,[29,30] and estimates of the effective reproductive number $R(t)$ with the new strain are increased by a factor of 1.4-1.8.[30] In this report, we used the proportion of contacts infected by an index patient as a measure of transmissibility and found a risk three times higher for a contact to be infected with the virus in the second period of study, in which variant B.1.1.7 was the dominant variant in Israel. In addition, during this period, B.1.1.7 was genotyped in two cases (out of two) from a large cluster of infection. Furthermore, the second period of the study is characterized by increased epidemic growth in the base with faster accumulation of cases in a shorter period, while rigorous COVID-19 mitigation strategies were already implemented. Our findings, which support higher infectivity, are in line with previous reports.[12–14] These finding emphasize the need for attentive public health efforts preventing "pandemic fatigue" (i.e., emphasizing social distancing, mandatory mask use, and hand hygiene) and controlling pandemic spread. Also, increased transmissibility might account for the higher than anticipated vaccination coverage needed in order to reach "herd immunity," as seen in Israel following January 2021, when a national-wide vaccination program was installed.[18,31] Higher transmissibility reported in this study could also be explained, in part by a behavioral component. A military vaccination campaign, which began on January 31, 2021, might have contributed to a false sense of protection, leading to decreased compliance with public health measures. Moreover, "pandemic fatigue" could affect adherence to instructions. However, since at that time, inside the base, and on a national level, pandemic wave was surging, leading to higher enforcement of public health restrictions, we believe those effects were somewhat mitigated. Another consideration when interpreting the results of higher infectivity is the eligibility for confirmatory testing. Testing criteria have changed throughout the pandemic, in accordance with international and national guidelines, potentially leading to different detection rates between periods. While the vast majority of cases in the study were detected under similar testing criteria, this should be taken into account.

Currently, there is no known difference in the clinical outcome associated with the B.1.1.7 variant. In this limited cohort, we found several differences in the clinical manifestation of disease in young healthy adults between two periods, the first before the identification of the B.1.1.7 variant in Israel and the second during the high national-wide prevalence of B.1.1.7. GI symptoms, loss of taste or smell, and fever, which were common manifestations in the first period, were significantly less commonly reported in the second period. On the other hand, a trend of more reports of sore throat, cough and fatigue during the second period was observed, with only the latter being statistically significant. These findings suggest that B.1.1.7 presentation might be much similar to "common-cold" and "seasonal flu," than previous variants. These changes in symptoms might be complementary to the molecular level explanation, as to why B.1.1.7 is more transmissible. Cough and colds might contribute to higher person-to-person transmisibility by increased viral shed to the environment. Our findings are in line with preliminary data from the United Kingdom, suggesting a decrease in reports of loss of taste or smell in areas with B.1.1.7 dominance and increased reported fatigue, sore throat, myalgia and fever.[23] In that report, however, no difference in GI symptoms was seen. The variance in the prevalence of GI symptoms reported in our study should be interpreted with caution, given the different time sections compared and the possible seasonality of other co-infections prevalent at the time, i.e., acute gastroenteritis in the summer. Moreover, it is possible that throughout the pandemic, a "reporting fatigue"[32] developed, having the potential to effect reports seen in the later period compared to the earlier one.

As seen in our results, period 2 population is characterized by a younger median age and increased mandatory military servants (including privates), compared with period 1. This suggests that although the base population has not changed with time, the cohort of positive cases did. Our cohort reflects a phenomenon seen in the entire IDF organization, in which disease spread entered Israel and the IDF from abroad.[33] Professional/career army personnel are older and are free to travel domestically and internationally. This is opposed to mandatory military service members, who are younger, with lower income, and are limited in travel, especially abroad. Thus, the first period contains much more professional army personnel who have imported the disease from abroad and raised the age median. Later in the pandemic (and in this study period 2), as there was widespread domestic transmission of the disease, we found an increase in confirmed cases among mandatory military servants, which comprise about 75% of the IDF population, that in turn drove the age median down.

Mandatory military servants, especially privates, have several unique characteristics, compared with professional army personnel who can effect disease transmission. Overall, we report an increased proportion of cases in individuals in mandatory duty, with the highest infection rate seen in newly enlisted trainees. Our findings are similar to previous reports in military setting[34] and can be explained by the condensed environment seen in boot camps and other types of basic trainings where soldiers usually work, study, and sleep in close proximity, all of which are known to affect SARS-CoV-2 transmission.[35,36] Privates are at a stage in which they usually acquire their military profession and share training in large groups (usually indoors) during daytime and share relatively crowded dorms at night. Our findings along with previous reports turn the spotlight on high infectivity affected by these factors. Based on these findings, we suggest further measures to mitigate propagation in military training camps and similar settings, such as the implementation of remote education using technological platforms, separation into smaller groups of enlistments, use of more staff and living facilities when possible, and decrease training duration to minimal time necessary.

This study includes a unique cohort comprised mainly young healthy adults, a subgroup that has not been studied extensively, but is the most common disease transmitting vector,[37–39] let alone when considering the vaccination effort worldwide focus first on the aged population.[40] Given the mandatory duty to serve in the IDF, the included population is highly diverse and representative of young Israeli adults. Additional strengths include the cost-free access to health services in the military, which is highly relevant in light of evidence linking socioeconomic and racial disparities to COVID-19 morbidity and mortality.[4] A major limitation of this study is the lack of sequencing to account for B.1.1.7 cases, but rather the reliance on variants' dominance according to national-wide studies at the time. In addition, changes in SARS-CoV-2 testing criteria throughout the pandemic can introduce a possible confounder. This limitation, however, is shared by many studies analyzing positive cases over time. Also, we could not control for differences in adherence to public health measures between periods; thus a behavioral component affecting some of the results is possible, especially with a military vaccination campaign in its early stages, which we cannot account for its effects on behavior. However, considering the pandemic surge in Israel and in the IDF during December 2020 and onward, public health efforts were on the rise, accentuating disease transmissibility, much more so, with uncertainty regarding vaccine's protection against B.1.1.7 at the time. Another shortcoming is the use of self-reported symptoms, which is prone to response bias, especially when epidemiological investigation is held with the individual aware of the diagnosis. Last, this cohort is limited in size and reflects a single institute's experience.

In conclusion, an outbreak of SARS-CoV-2 in young healthy adults, in a military setting, during a period with a very high national-wide B.1.1.7 prevalence, is characterized by a decreased prevalence of fever, loss of taste or smell and GI symptoms, increased reports of fatigue, and high disease transmissibility for each index case. As SARS-CoV-2 continue to mutate, emerging variants continue to challenge every aspect of pandemic control. Extensive and ongoing studies of phenotypic variance and infectivity of current and previous variants are of importance in formulating public health response and testing criteria. A growing body of evidence of symptomatology of previous variants, integrated with molecular level changes, might assist in predicting the behavior of future variants and aid the health community to catch up with this constantly changing virus.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *Military Medicine* online.

FUNDING

None declared.

CONFLICT OF INTEREST STATEMENT

None declared.

ETHICAL APPROVAL

The institutional review board of the IDF approved this study (protocol number 2092-2020) and waived the requirement for written informed consent based on preserving participants' anonymity.

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