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Seroprevalence of SARS-CoV-2 in Palestine: a cross-sectional seroepidemiological study

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Abstract

Objectives

Seroprevalence rates are important indicators to the epidemiology of COVID-19 and the extent of the pandemic given the existence of asymptomatic cases. The purpose of this study is to assess the seroprevalence rate in the Palestinian population residing in the West Bank.

Setting

The study involved 1355 participants from 11 governorates, including 112 localities in the West Bank, Palestine.

Participants

Blood samples were collected between 15th June 2020 and 30th June 2020 from 1355 individuals from randomly selected households in the West Bank in addition to 1136 individuals visiting Palestinian medical laboratories between the 1st May 2020 and 9th July 2020 for a *routine checkup*.

Primary and secondary outcome measures

Out of the 2491 blood samples collected, serological tests for 2455 adequate serum samples were done using an Immunoassay for qualitative detection of antibodies against SARS-CoV-2. seroprevalence was estimated as the proportion of individuals who had a positive result in the total SARS-CoV-2 antibodies in the immunoassay

Results

The random sample of Palestinians living in the West Bank yielded 0% seroprevalence with 95% CI [0,0.0036], while the lab referrals sample yielded an estimated seroprevalence of 0.354% with 95% CI [0.0011,0096].

Conclusions

Our results indicate that as of July 2020, seroprevalence in Palestine persist low and is inadequate to provide herd immunity, emphasizing the need to maintain health measures to keep the outbreak under control. Population-based *seroprevalence studies are to be conducted periodically to monitor the* SARS-CoV-2 seroprevalence in Palestine and inform policy makers about the efficacy of their surveillance system.

Strengths and limitations of this study

Strenghths:

1- The random selection of households residents collected between 15th June 2020 and 30th June 2020. The clusters were selected using probability proportional to size (PPS) sampling.

2- The study also included 1136 participants from Medicare laboratory referrals between 1st May 2020 and 9th July 2020 in 16 branches in the West Bank, which had good representation of females as well as children

Limitations:

1- Low representation in females represented in the random sample, the samples from female were more difficult to obtain due to a cultural inhibition regarding allowing nurses to enter the households.

2- The random sample did not include children under the age of 15 to avoid anxiety due to fear of needles in the study to eliminate personal fears due to blood withdrawl.

3- Our study only detected Sars-Cov2 antibodies. However, it is important to recognize that cellular immunity may play a role in providing immunity against SARS-CoV-2 reinfection[18]. Further studies aimed at testing cellular immunity are important.

Introduction

Coronavirus disease 2019, known as COVID-19, is an infectious respiratory disease caused by novel coronavirus SARS-CoV-2 [1]. Since its emergence in Wuhan, China in December 2019 [2], SARS-CoV-2 has spread rapidly around the globe, ultimately being declared by the World Health Organization (WHO) as a global pandemic [3,4] and new cases and deaths are being reported daily[5].

Most authorities rely on PCR testing results to estimate number of COVID-19 cases and make up-to-date decisions [6]. Thus, numbers of patients tested positive for SARS-CoV-2 through PCR testing, symptomatic patients, those admitted to hospitals, or deceased from Cobvid-19 are updated on a daily basis. However, the data may exclude a fraction of the population with previous mild or asymptomatic COVID-19that has not been tested by PCR . The proportion of the population who have overcome the infection without being noticed can probably be approximated by testing for antibodies against SARS-CoV-2. Antibodies may confer immunity to repeat infection and a high proportion of immune individuals can attenuate the epidemic. Measures of anti-SARS-CoV-2 seroprevalence can also be used to estimate the clinical impact of COVID-19. To this effect, several serological surveys of SARS-CoV-2 have been done worldwide [7–16].

Objective:

There is lack of data on the the percentage of undiagnosed Palestinian population with previous mild or asymptomatic COVID-19. Prevalence of COVID-19 among Palestinian remains unknown and many are concerned about this uncertainty. To this end, we conducted a population cross sectional based seroepidemiological study to assess the spread of SARS-CoV-2 throughout the West Bank. The study included 2491 individuals, designed to be representative by cities (1355

from randomly selected households and 1136 from laboratory referrals). Elecsys® Anti-SARS-CoV-2 testing was done on 2455 adequate serum samples. Here, we describe the study design and the results of the first wave of the study.

Methods

Study design and participants

The study conducted is a cross-sectional serologic testing study aimed to investigate seropositivity for SARS-CoV-2 in the non-institutionalized Palestinian population residing in the West Bank.

The study involved 1355 participants from 11 governorates, including 112 localities (supplementary table 1). 1395 households were selected using 3-stage cluster sampling. The cluster of households or census track is considered to be a geographic location that is comprised of approximately 100 households. The process for conducting cluster sampling was carried as follows : (1) Selecting a cluster of households, (2) Selecting 10 households randomly from each cluster and (3) Selecting a person at random from the selected household. The clusters were selected using probability proportional to size (PPS) sampling (Table 1).

To select the number of clusters within each population location: (1) we calculated the sampling interval which equals the total number of households divided by the total number of clusters need to be selected by the sample say for example (m). So the sampling interval SI= N/m, where N is the total number of households. (2) selected a random number R0 between 0 and SI. (3) calculated Ri as R0+i*SI, a cluster is selected in Li if Ri belongs to the interval [Ci-1, Ci].

Field work was carried out between 15th[th] June 2020 and 30[th] June 2020 by a team of registered nurses, laboratory technicians, nursing students and laboratory technician students from the Arab American University following standardized health protocols (World Health, 2020) .

The study also included 1136 participants from Medicare laboratory referrals between 1[st] May 2020 and 9[th] July 2020 in 16 branches in the West Bank (supplementary table 2) .

Participants donated a blood sample for antibodies detection. Blood samples were centrifuged and serum was separated, labelled, stored at -20C at AAUP laboratory until it was used.

Detection of antibodies

Serological tests for 2455 adequate serum samples were done using an Immunoassay for the qualitative detection of antibodies against SARS-CoV-2 (Elecsys® Anti-SARS-CoV-2**)** in human serum by using the Cobas analyzer cobas e 411 (Roche) . The assay uses a recombinant protein representing the nucleocapsid (N) antigen for the determination of antibodies against SARS-CoV-2 with testing time of 18 minutes. We included 6 samples from recovered cases with detected SARS-COV2 antibodies as a positive control.

Statistical Analysis

We estimated seroprevalence as the proportion of individuals who had a positive result in the total SARS-CoV-2 antibodies in the immunoassay.

We used Wilson Method With Continuity Correction and Boundary Truncation (WCCBT) to construct 95% CI for the population parameter of seroprevalence [17] .

Patients and public involvement

The study involved 1355 participants from 11 governorates, including 112 localities and included 1136 participants from Medicare laboratory referrals. The development of the research question and outcome measures was based on the public priorities to know the seroprevalnce in the Palestinian community. Approval from National ethical committee was obtained (PHRC/HC/737/20). Written informed consent was obtained from the 1355 study participants and approvals were obtained from Medicare laboratories for samples to be tested. Participants \ were notified of the results of the tests.

Results

Of the 1395 eligible individuals residing in households selected using 3-stage cluster sampling, 1355 participants agreed to participate in the study. The proportion of females was lower compared to males (137, 1218 respectively) including 349 in age group (15-24), 314 in age group (25-34), 377 in age group (35-49) and 315 in age group (50+). Out of the 1355 blood samples collected, 1319 serum samples were adequate for testing. None of the tested specimens revealed presence of antibodies against SARS-CoV-2. A 95% CI for the population parameter of seroprevalence was [0,0.0036].

Of the1136 participants from Medicare laboratory referrals in 16 branches. The proportion of males was lower than females (395, 741 respectively) including 71 in age group lower less than 15 , 173 in age group (15-24), 297 tests in age group (25-34), 290 in age group (35-49) and 305 in age group (50+) . All serum samples were adequate for testing. Out of the 1136 tested participants, 4 revealed antibodies against Sars-CoV-2 with 95% CI [0.0011,0096].

Discussion

To our knowledge, this is the first SARS-CoV-2 seroprevalence study in Palestine. The findings from this seroprevalence study for SARS-CoV-2 indicate that the estimated seroprevalence of the total SARS-COV2 antibodies persist low. The random sample of Palestinians living in the West Bank yeilded 0% seroprevalence with 95% CI [0,0.0036], while the lab referrals sample yielded an estimated seroprevalence of 0.354% with 95% CI [0.0011,0096]. Seroprevelance in Palestine is very close to that identified in Jordan (0% prevalence) [15], a neighboring country, which was explained to be due to the strict closures implemented by the Jordanian government and the eventual curtailing of infections in Jordan. In comparison to other countries like Spain, Italy. Japan India, Los Angeles, Germany, Switzerland the seroprevalence in Palestine is low [7–16]. It is, however, noteworthy that a comparison with other countries may be problematic due to the timing and the stage of the pandemic which may vary affecting the seroprevalence estimates.

A key strength of our study is the random selection of households residents collected between 15th June 2020 and 30th June 2020. The clusters were selected using probability proportional to size (PPS) sampling. This technique ensures getting self-weighting sample which can be used to produce unbiased estimators for the parameters of interest. However, samples from female were more difficult to obtain due to a cultural inhibition regarding allowing nurses to enter the households. Also, random sample did not include children under the age of 15 to avoid anxiety due to fear of needles in the study to eliminate personal fears due to blood withdrawl.

As for the lab referals sample, it represents the population of the lab referals between the 1st May 2020 and 9th July 2020. The seroprevalence in this sample was 4 positive cases out of the 1136 samples tested. Since the seroprevalence within the lab referral population is close to zero , we

used Wislon Method With Continuity Correction and Truncation (WCCBT) to construct a 95% confidence intervale for the population parameter of seroprevalence [0.0011,0096].

Our study only detected Sars-Cov2 antibodies. However, it is important to recognize that cellular immunity may play a role in providing immunity against SARS-CoV-2 reinfection[18]. Further studies aimed at testing cellular immunity are important. It is also noteworthy that previous studies have indicated that asymptomatic individuals were reported to have a weaker immune response to SARS-CoV-2 infection and a higher percentage of asymptomatic individuals became seronegative when compared to symptomatic individuals in the early recovering phases. The reduction in neutralizing antibody levels may have implications for immunity strategy and serological surveys [19].

In conclusion, our study provides estimates of SARS-CoV-2 seroprevalence in Palestine. Our estimate is low indicating that as of July 2020 the population does not have herd immunity. In this situation, health measures have to be taken to keep the outbreak under control. In order to monitor the SARS-CoV-2 seroprevalence in Palestine and inform policy makers about the efficacy of their survalance system, conducting population-based seroprevalence studies on a regular basis is important.

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Conflict of Interest Disclosures

No authors reported disclosures.

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Authors contribution

Research design: Nouar Qutob, Zaidoun Salah, Faisal Awartani

Field work coordination: Mohammad Asia, Imad Abu Khader

Data analysis: Faisal Awartani

Manuscript writing: Nouar Qutob

Manuscript revisions: Nouar Qutob, Faisal Awartani, Zaidoun Salah, Mohammad Asia

Methadology and lab work: Nouar Qutob, Khaled Herzallah, Nadeen Balqis, Husam Sallam

References

1. Mayo clinic. oronavirus disease 2019 (COVID-19).

2. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *J Med Virol*. 2020;92(4):401-402. doi:10.1002/jmv.25678

3. World Health Organization. *Novel Coronavirus(2019-NCoV), Situation Report - 12*.; 2020.

4. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health — The latest 2019 novel coronavirus outbreak in Wuhan, China The. 2020;(January).

5. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU).

6. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA - J Am Med Assoc*. 2020;2019:2019-2020. doi:10.1001/jama.2020.4683

7. Snoeck CJ, Vaillant M, Abdelrahman T, et al. Prevalence of SARS-CoV-2 infection in the Luxembourgish population the CON-VINCE study. *Medrxiv*. 2020:2020.05.11.20092916. doi:10.1101/2020.05.11.20092916

8. Wu X, Fu B, Chen L, Feng Y. Serological tests facilitate identification of asymptomatic SARS-CoV-2 infection in Wuhan, China. *J Med Virol*. 2020:2-3. doi:10.1002/jmv.25904

9. Bryan A, Pepper G, Wener MH, et al. Performance Characteristics of the Abbott Architect

SARS-CoV-2 IgG Assay and Seroprevalence in Boise, Idaho. *J Clin Microbiol*. 2020;(May). doi:10.1128/JCM.00941-20

10. Stringhini S, Wisniak A, Piumatti G, et al. Repeated seroprevalence of anti-SARS-CoV-2 IgG antibodies in a population-based sample from Geneva, Switzerland. *medRxiv*. 2020:2020.05.02.20088898. doi:10.1101/2020.05.02.20088898

11. Valenti L, Bergna A, Pelusi S, et al. SARS-CoV-2 seroprevalence trends in healthy blood donors during the COVID-19 Milan outbreak. *medRxiv*. 2020:2020.05.11.20098442. doi:10.1101/2020.05.11.20098442

12. Shakiba M, Hashemi Nazari SS, Mehrabian F, Rezvani SM, Ghasempour Z, Heidarzadeh A. Seroprevalence of COVID-19 virus infection in Guilan province, Iran. *medRxiv*. 2020:2020.04.26.20079244. doi:10.1101/2020.04.26.20079244

13. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet (London, England)*. 2020;6736(20):1-11. doi:10.1016/S0140-6736(20)31483-5

14. Stadlbauer D, Amanat F, Chromikova V, et al. SARS-CoV-2 Seroconversion in Humans: A Detailed Protocol for a Serological Assay, Antigen Production, and Test Setup. *Curr Protoc Microbiol*. 2020;57(1):2425-2427. doi:10.1002/cpmc.100

15. Sughayer MA, Mansour A, Nuirat A Al, Souan L, Ghanem M, Siag M. Covid-19 Seroprevalence rate in healthy blood donors from a community under strict lockdown measures. *medRxiv*. 2020:2020.06.06.20123919. doi:10.1101/2020.06.06.20123919

16. Hains DS, Schwaderer AL, Carroll AE, Starr MC, Wilson AC. Seroprevalence of SARS-

CoV-2 – Specific Antibodies Among Adults in Los Angeles County , California , on April 10-11 , 2020. 2020;323(23):2425-2427. doi:10.1002/cpmc.100

17. Sakthivel Sivam SM. Everything or Nothing - A Better Confidence Intervals for Binomial Proportion in Clinical Trial Data Analysis . Sakthivel Sivam , Quartesian LLC , Princeton , New Jersey Subbiah Meenakshisundaram , L . N Government College , Ponneri , India. 2016;(2014).

18. Sekine T, Perez-Potti A, Rivera-Ballesteros O, et al. Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19. *bioRxiv*. 2020:2020.06.29.174888. doi:10.1101/2020.06.29.174888

19. Quan-Xin Long 1, 8, Xiao-Jun Tang2, 8, Qiu-Lin Shi2, 8, Qin Li3, 8, Hai-Jun Deng 1, 8 JY, Hu1 J-L, Xu2 W, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med*. 2020.

Supplementary Table 1: Governorates and localities included in the households sample

Governorate	Locality
Jenin	Sir
Jenin	Anza
Jenin	Al Araqa
Jenin	Al Mughayyir
Jenin	Al Fandaqumiya
Jenin	Al Judeida
Jenin	Ajja
Jenin	Birqin
Jenin	Meithalun
Jenin	Jaba
Jenin	Silat al Harithiya
Jenin	Arraba
Jenin	Yabad
Jenin	Al Yamun
Jenin	Qabatiya
Jenin	Jenin
Tubas	Ras al Faraa
Tubas	Aqqaba
Tubas	Tammun
Tubas	Tubas
Tulkarm	Kafa
Tulkarm	Kafr Jammal
Tulkarm	Kafr al Labad
Tulkarm	Nur Shams Camp
Tulkarm	Bala
Tulkarm	Tulkarm Camp
Tulkarm	Attil
Tulkarm	Tulkarm
Nablus	Iraq Burin
Nablus	Qusin
Nablus	As Sawiya
Nablus	Majdal Bani Fadil
Nablus	Sabastiya
Nablus	Ein Beit el Ma Camp
Nablus	Beit Dajan
Nablus	Qusra
Nablus	Askar Camp)al Qadeem(
Nablus	Awarta
Nablus	Asira ash Shamaliya
Nablus	Aqraba

Nablus	Beit Furik
Nablus	Balata Camp
Nablus	Nablus
Qalqiliya	Kafr Laqif
Qalqiliya	Jinsafut
Qalqiliya	Sanniriya
Qalqiliya	Azzun
Qalqiliya	Qalqiliya
Salfit	Deir Istiya
Salfit	Haris
Salfit	Biddya
Salfit	Salfit
Ramallah & Al-Bireh	Shabtin
Ramallah & Al-Bireh	Ein Arik
Ramallah & Al-Bireh	Beitin
Ramallah & Al-Bireh	Ein Yabrud
Ramallah & Al-Bireh	Arura
Ramallah & Al-Bireh	Beitillu
Ramallah & Al-Bireh	Deir Abu Mashaal
Ramallah & Al-Bireh	Khirbet Abu Falah
Ramallah & Al-Bireh	Beit Ur at Tahta
Ramallah & Al-Bireh	Shuqba
Ramallah & Al-Bireh	Qibya
Ramallah & Al-Bireh	Al Jalazun Camp
Ramallah & Al-Bireh	Beituniya
Ramallah & Al-Bireh	Ramallah
Ramallah & Al-Bireh	Al Bireh
Jericho & Al-Aghwar	Ein as Sultan Camp
Jericho & Al-Aghwar	Jericho)Ariha(

Jerusalem	Ash Sheikh Sad
Jerusalem	Beit Surik
Jerusalem	As Sawahira ash Sharqiya
Jerusalem	Hizma
Jerusalem	Qalandiya Camp
Jerusalem	Ar Ram & Dahiyat al Bareed
Jerusalem	Anata
Jerusalem	Al Eizariya
Bethlehem	Al Masara
Bethlehem	Wadi Rahhal
Bethlehem	Dar Salah
Bethlehem	Husan
Bethlehem	Hindaza and Bureidaa
Bethlehem	Nahhalin
Bethlehem	Ad Duheisha Camp
Bethlehem	Ad Doha
Bethlehem	Beit Sahur
Bethlehem	Beit Jala
Bethlehem	Beit Fajjar
Bethlehem	Bethlehem (Beit Lahm)
Hebron	An Najada
Hebron	Beit ar Rush al Fauqa
Hebron	Shuyukh al Arrub
Hebron	Al Burj and Al Bira
Hebron	Nuba
Hebron	Al Fawwar Camp
Hebron	Beit Kahil
Hebron	Kharas
Hebron	Beit Awwa
Hebron	Beit Ula
Hebron	Taffuh
Hebron	Beit Ummar
Hebron	Surif
Hebron	Tarqumiya
Hebron	Sair
Hebron	Bani Naim
Hebron	Idhna
Hebron	As Samu
Hebron	Halhul
Hebron	Adahiriya
Hebron	Dura
Hebron	Yatta

Hebron	Hebron (Al Khalil)

Supplementary Table 2: Governorates and localities included in the lab referrals sample

Governorate	Locality
Jericho	Jericho
Hebron	Dura
Hebron	Yatta
Hebron	Hebron (Al Khalil)
Hebron	Adahiriya
Bethany	Bethany
Bethlehem	Bethlehem
Jenin	Jenin
Ramallah	Ramallah
Ramallah	Silwad
Tubas	Tubas
Tulkarem	Tulkarem
Qalqiliah	Qalqiliah
Nablus	Nablus
Salfit	Bidia
Salfit	Salfit

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Seroprevalence of SARS-CoV-2 the West Bank region of Palestine **a cross-sectional seroepidemiological study**

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Keywords: seroprevalence, Sars-cov-2, Palestine, immunity, covid-19

Word count: 2602

Abstract

Objectives

Seroprevalence rates are important indicators to the epidemiology of COVID-19 and the extent of the pandemic given the existence of asymptomatic cases. The purpose of this study is to assess the seroprevalence rate in the Palestinian population residing in the West Bank.

Setting

The study involved 1355 participants from 11 governorates, including 112 localities in the West Bank, Palestine.

Participants

Blood samples were collected between 15th June 2020 and 30th June 2020 from 1355 individuals from randomly selected households in the West Bank in addition to 1136 individuals visiting Palestinian medical laboratories between the 1st May 2020 and 9th July 2020 for a routine checkup.

Primary and secondary outcome measures

Out of the 2491 blood samples collected, serological tests for 2455 adequate serum samples were done using an Immunoassay for qualitative detection of antibodies against SARS-CoV-2. seroprevalence was estimated as the proportion of individuals who had a positive result in the total SARS-CoV-2 antibodies in the immunoassay

Results

The random sample of Palestinians living in the West Bank yielded 0% seroprevalence with 95% and an adjusted confidence interval [0 , 0.0043], while the lab referrals sample yielded an estimated seroprevalence of 0.354% with 95% and an adjusted confidence interval [0.001325 , 0.011566].

Conclusions

Our results indicate that as of July 2020, seroprevalence in Palestine persist low and is inadequate to provide herd immunity, emphasizing the need to maintain health measures to keep the outbreak under control. Population-based seroprevalence studies are to be conducted periodically to monitor the SARS-CoV-2 seroprevalence in Palestine and inform policy makers about the efficacy of their surveillance system.

Strengths and limitations of this study

Strenghths:

1- The random selection of households residents collected between 15th June 2020 and 30th June 2020. The clusters were selected using probability proportional to size (PPS) sampling.

2- The study also included 1136 participants from Medicare laboratory referrals between 1st May 2020 and 9th July 2020 in 16 branches in the West Bank, which had good representation of females as well as children

Limitations:

1- Low representation in females represented in the random sample, the samples from female were more difficult to obtain due to a cultural inhibition regarding allowing nurses to enter the households.

2- The random sample did not include children under the age of 15 to avoid anxiety due to fear of needles in the study to eliminate personal fears due to blood withdrawl.

3- Our study only detected Sars-Cov2 antibodies. However, it is important to recognize that cellular immunity may play a role in providing immunity against SARS-CoV-2 reinfection[1]. Further studies aimed at testing cellular immunity are important.

4- It was previously reported that antibodies against SARS-CoV-2 may drop or even disappear in patients with mild Covid-19, which may have led to the inability to detect antibodies in a few previously positive cases

Introduction

Coronavirus disease 2019, known as COVID-19, is an infectious respiratory disease caused by novel coronavirus SARS-CoV-2 [2]. Since its emergence in Wuhan, China in December 2019 [3], SARS-CoV-2 has spread rapidly around the globe. A global pandemic was declared by the World Health Organization (WHO) [4,5] and new cases and deaths are being reported daily [6].

Most authorities rely on PCR testing results to estimate number of COVID-19 cases and make up-to-date decisions [7]. Thus, numbers of patients tested positive for SARS-CoV-2 through PCR testing, symptomatic patients, those admitted to hospitals, or deceased from Cobvid-19 are updated on a daily basis. However, the data may exclude a fraction of the population with previous mild or asymptomatic COVID-19that has not been tested by PCR . The proportion of the population who have overcome the infection without being noticed can probably be approximated by testing for antibodies against SARS-CoV-2. Antibodies may confer immunity to repeat infection and a high proportion of immune individuals can attenuate the epidemic. Measures of anti-SARS-CoV-2 seroprevalence can also be used to estimate the clinical impact of COVID-19. To this effect, several serological surveys of SARS-CoV-2 have been done worldwide [8–17].

Objective:

There is lack of data on the the percentage of undiagnosed Palestinian population with previous mild or asymptomatic COVID-19. Prevalence of COVID-19 infections among Palestinians residing in the West Bank remains unknown and many are concerned about this uncertainty. To this end, we conducted a population cross sectional based seroepidemiological study to assess the spread of SARS-CoV-2 throughout the West Bank. The study included 2491 individuals, designed to be representative by cities (1355 from randomly selected households and 1136 from laboratory

referrals). Elecsys® Anti-SARS-CoV-2 testing was done on 2455 adequate serum samples. Here, we describe the study design and the results of the first wave of the study.

Methods

Study design and participants

The study conducted is a cross-sectional serologic testing study aimed to investigate seropositivity for SARS-CoV-2 in the non-institutionalized Palestinian population residing in the West Bank.

The study involved 1355 participants from 11 governorates, including 112 localities (supplementary table 1). We used 3-stage cluster sampling to select 1395 households. The cluster of households or census track is considered to be a geographic location that is comprised of approximately 100 households. The process for conducting cluster sampling was carried as follows : (1) Selecting a cluster of households, (2) Selecting 10 households randomly from each cluster and (3) Selecting a person at random from the selected household. The clusters were selected using probability proportional to size (PPS) sampling (Table 1).

Table 1: The PPS sampling algorithm

Location	# of households in the location	Cumulative
L1	X1	C1=X1
L2	X2	C2=X1+X2

L3	X3	C3=X1+X2+X3
.	.	.
.	.	.
.	.	.
Lk-1	Xk-1	Ck-1=X1+X2+…+Xk-1
Lk	Xk	Ck = X1+X2+…+Xk

To select the number of clusters within each population location: (1) we calculated the sampling interval which equals the total number of households divided by the total number of clusters need to be selected by the sample say for example (m). So the sampling interval SI= N/m, where N is the total number of households. (2) selected a random number R0 between 0 and SI. (3) calculated Ri as R0+i*SI, a cluster is selected in Li if Ri belongs to the interval [Ci-1, Ci].

Field work was carried out between 15thth June 2020 and 30th June 2020 by a team of registered nurses, laboratory technicians, nursing students and laboratory technician students from the Arab American University following standardized health protocols [18].

The study also included 1136 participants from Medicare® medical laboratories network referrals between 1st May 2020 and 9th July 2020 in 16 branches in the West Bank (supplementary table 2).

Participants donated a blood sample for antibodies detection. Blood samples were centrifuged and serum was separated, labelled, stored at -20C at AAUP laboratory until it was used.

Detection of antibodies

Serological tests for 2455 adequate serum samples were done using an Immunoassay for the qualitative detection of antibodies against SARS-CoV-2 (Elecsys® Anti-SARS-CoV-2**)** in human serum by using the Cobas analyzer cobas e 411 (Roche) . The assay uses a recombinant protein representing the nucleocapsid (N) antigen for the determination of antibodies against SARS-CoV-2 with testing time of 18 minutes. We included 6 samples from recovered cases with detected SARS-COV2 antibodies as a positive control.

Statistical Analysis

We estimated seroprevalence as the proportion of individuals who had a positive result in the total SARS-CoV-2 antibodies in the immunoassay.

We used Wilson Method With Continuity Correction and Boundary Truncation (WCCBT) to construct 95% CI for the population parameter of seroprevalence [19] .

We calculated the adjusted confidence of interval. Since the specificity of the kit used for the antibodies test is 100% and 83% respectively [20], we adjusted the confidence interval for seroprevalence according to the following transformation: Adjusted lower confidence limit= max[0, {a-(1-sp)}/(sp+se-1)] and adjusted upper confidence limit=min[1, {b-(1-sp)}/(sp+se-1)] [21].

Patients and public involvement

The study involved 1355 participants from 11 governorates, including 112 localities and included 1136 participants from Medicare® laboratories referrals. The development of the research question and outcome measures was based on the public priorities to know the seroprevalnce in the Palestinian community. Approval from National ethical committee was obtained (PHRC/HC/737/20). Written informed consent was obtained from the 1355 study participants and approvals were obtained from Medicare® laboratories for samples to be tested. Participants \ were notified of the results of the tests.

Results

Of the 1395 eligible individuals residing in households selected using 3-stage cluster sampling, 1355 participants agreed to participate in the study. The proportion of females was lower compared to males (137, 1218 respectively) including 349 in age group (15-24), 314 in age group (25-34), 377 in age group (35-49) and 315 in age group (50+). (Figure 1). The majority of the participants did not report having symptoms in the last three months nor prevailing chronic diseases (supplementary table 3 and 4). None of the tested specimens revealed presence of antibodies against SARS-CoV-2. A 95% CI for the population parameter of seroprevalence was [0.0, 0.0036]. A 95% CI for the population parameter of seroprevalence was [0.0, 0.0036], and an adjusted confidence interval of [0, 0.0043].

Out of the 1355 blood samples collected, 1319 serum samples were adequate for testing. None of the tested specimens revealed presence of antibodies against SARS-CoV-2. A 95% CI for the population parameter of seroprevalence was [0,0.0036].

Of the1136 participants from Medicare laboratory referrals in 16 branches. The proportion of males was lower than females (395, 741 respectively) including 71 in age group lower less than 15 , 173 in age group (15-24), 297 tests in age group (25-34), 290 in age group (35-49) and 305 in age group (50+) (Figure 2). Records of symptoms and chronic diseases were unattainable. Out of the 1136 tested participants, 3 males, ages 38, 58, 59 and 1 female, age 40 revealed antibodies against SARS-CoV-2, with 95% CI [0.0011,0.0096] and an adjusted confidence interval of [0.001325, 0.011566].

All serum samples were adequate for testing. Out of the 1136 tested participants, 4 revealed antibodies against Sars-CoV-2 with 95% CI [0.0011,0096].

Discussion

To our knowledge, this is the first SARS-CoV-2 seroprevalence study in Palestine. The findings from this seroprevalence study for SARS-CoV-2 indicate that the estimated seroprevalence of the total SARS-CoV-2 antibodies persist low as of mid of June. The random sample of Palestinians living in the West Bank yielded 0% seroprevalence with 95% and an adjusted confidence interval of [0, 0.0043], while the lab referrals sample yielded an estimated seroprevalence of 0.354% with 95% and an adjusted confidence [0.001325, 0.011566].

The low SARS-CoV-2 antibody prevalence in our population can be explained by the imposed total lockdown in the first three months when cases were under control and only reached around 800 cases by May. Seroprevalence in Palestine is very close to that identified in Jordan (0% prevalence) [16], a neighboring country, which was explained to be due to the strict closures implemented by the Jordanian government and the eventual curtailing of infections in Jordan.

Also, Seroprevalence in Maine and Montana was 0.4% and 0.5% respectively by end of August 2020 [22]. In comparison to other countries like Spain, Italy. Japan India, Los Angeles, Germany, Switzerland the seroprevalence in Palestine is low [8–17]. Similarly, the seroprevalence among Palestinians residing in the West Bank was shown to be lower than that in Israel as reported in the first conducted serological study of 1,700 tests. The study suggested that 2.5 percent of the Israeli population, have had the coronavirus[23]. It is, however, noteworthy that a comparison with other countries may be problematic due to the timing and the stage of the pandemic which may vary affecting the seroprevalence estimates.

A key strength of our study is the random selection of household's residents collected between 15th June 2020 and 30th June 2020. The clusters were selected using probability proportional to size (PPS) sampling. This technique ensures getting self-weighting sample which can be used to produce unbiased estimators for the parameters of interest. However, samples from females were more difficult to obtain due to a cultural inhibition regarding allowing nurses to enter the households. Also, random samples did not include children under the age of 15 to avoid anxiety due to fear of needles in the study to eliminate personal fears due to blood withdrawal.

As for the lab referrals sample, it represents the population of the lab referrals between the 1st May 2020 and 9th July 2020. The seroprevalence in this sample was 4 positive cases out of the 1136 samples tested. Since the seroprevalence within the lab referral population is close to zero, we used Wislon Method With Continuity Correction and Truncation (WCCBT) to construct a 95% confidence interval for the population parameter of seroprevalence [0.0011,0096]. In comparison to household samples that were collected between 15th-30th of June, laboratory referral samples

include a good representation of females and children below the age of 15 (Figure 2). Also, samples were collected starting from May 1st, which may better represent the small peaks of SARS-CoV-2 reported cases in Palestine and thus explain the presence of few positive samples in comparison to null in household samples.

Our study only detected SARS-CoV-2 antibodies. It was previously reported that antibodies against SARS-CoV-2 may drop or even disappear in patients with mild Covid-19, which may have led to the inability to detect antibodies in a few previously positive cases [24,25] . Also, it is important to recognize that cellular immunity may play a role in providing immunity against SARS-CoV-2 reinfection[18]. Further studies aimed at testing cellular immunity are important. It is also noteworthy that previous studies have indicated that asymptomatic individuals were reported to have a weaker immune response to SARS-CoV-2 infection and a higher percentage of asymptomatic individuals became seronegative when compared to symptomatic individuals in the early recovering phases. The reduction in neutralizing antibody levels may have implications for immunity strategy and serological surveys [26,27].

In conclusion, our study provides estimates of SARS-CoV-2 seroprevalence in Palestine. Our results reflect the seroprevalence as of mid of June. It is noteworthy that on May 25th, the government of Palestine eased the restrictions following a decline in cases which led to a surge in cases beginning of July, with the epicenter of the epidemic in Hebron accounting for over 70 % of active cases implying a possible increase in seroprevalence after July. In this situation, health measures have to be taken to keep the outbreak under control. In order to monitor the SARS-CoV-2 seroprevalence in Palestine and inform policy makers about the efficacy of their surveillance system, conducting population-based seroprevalence studies on a regular basis is important.

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Conflict of Interest Disclosures

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Authors contribution

Research design: Nouar Qutob, Zaidoun Salah, Faisal Awartani

Field work coordination: Mohammad Asia, Imad Abu Khader

Data analysis: Faisal Awartani

Manuscript writing: Nouar Qutob

Manuscript revisions: Nouar Qutob, Faisal Awartani, Zaidoun Salah, Mohammad Asia

Methadology and lab work: Nouar Qutob, Khaled Herzallah, Nadeen Balqis, Husam Sallam

Data sharing

Data are available upon reasonable request

Figure Legends

Figure 1: (a) Age and (b) gender distribution of the 1355 participants from Palestinian households in the West Bank. Blood samples were collected between 15th June 2020 and 30th June from the participants.

Figure 2: (a) Age and (b) Gender distribution of the 1136 participants visiting Medicare laboratories between the 1st May 2020 and 9th July 2020 for a routine checkup.

References

1. Sekine T, Perez-Potti A, Rivera-Ballesteros O, et al. Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19. *bioRxiv*. 2020:2020.06.29.174888. doi:10.1101/2020.06.29.174888

2. Mayo clinic. oronavirus disease 2019 (COVID-19).

3. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *J Med Virol*. 2020;92(4):401-402. doi:10.1002/jmv.25678

4. World Health Organization. *Novel Coronavirus(2019-NCoV), Situation Report - 12*.; 2020.

5. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health — The latest 2019 novel coronavirus outbreak in Wuhan, China The. 2020;(January).

6. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU).

7. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA - J Am Med Assoc*. 2020;2019:2019-2020. doi:10.1001/jama.2020.4683

8. Snoeck CJ, Vaillant M, Abdelrahman T, et al. Prevalence of SARS-CoV-2 infection in the Luxembourgish population the CON-VINCE study. *Medrxiv*. 2020:2020.05.11.20092916. doi:10.1101/2020.05.11.20092916

9. Wu X, Fu B, Chen L, Feng Y. Serological tests facilitate identification of asymptomatic SARS-CoV-2 infection in Wuhan, China. *J Med Virol*. 2020:2-3. doi:10.1002/jmv.25904

10. Bryan A, Pepper G, Wener MH, et al. Performance Characteristics of the Abbott Architect SARS-CoV-2 IgG Assay and Seroprevalence in Boise, Idaho. *J Clin Microbiol*. 2020;(May). doi:10.1128/JCM.00941-20

11. Stringhini S, Wisniak A, Piumatti G, et al. Repeated seroprevalence of anti-SARS-CoV-2 IgG antibodies in a population-based sample from Geneva, Switzerland. *medRxiv*. 2020:2020.05.02.20088898. doi:10.1101/2020.05.02.20088898

12. Valenti L, Bergna A, Pelusi S, et al. SARS-CoV-2 seroprevalence trends in healthy blood donors during the COVID-19 Milan outbreak. *medRxiv*. 2020:2020.05.11.20098442. doi:10.1101/2020.05.11.20098442

13. Shakiba M, Hashemi Nazari SS, Mehrabian F, Rezvani SM, Ghasempour Z, Heidarzadeh A. Seroprevalence of COVID-19 virus infection in Guilan province, Iran. *medRxiv*. 2020:2020.04.26.20079244. doi:10.1101/2020.04.26.20079244

14. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet (London, England)*. 2020;6736(20):1-11. doi:10.1016/S0140-6736(20)31483-5

15. Stadlbauer D, Amanat F, Chromikova V, et al. SARS-CoV-2 Seroconversion in Humans: A Detailed Protocol for a Serological Assay, Antigen Production, and Test Setup. *Curr Protoc Microbiol*. 2020;57(1):2425-2427. doi:10.1002/cpmc.100

16. Sughayer MA, Mansour A, Nuirat A Al, Souan L, Ghanem M, Siag M. Covid-19 Seroprevalence rate in healthy blood donors from a community under strict lockdown measures. *medRxiv*. 2020:2020.06.06.20123919. doi:10.1101/2020.06.06.20123919

17. Hains DS, Schwaderer AL, Carroll AE, Starr MC, Wilson AC. Seroprevalence of SARS-CoV-2 – Specific Antibodies Among Adults in Los Angeles County , California , on April 10-11 , 2020. 2020;323(23):2425-2427. doi:10.1002/cpmc.100

18. World Health Organization. Ethical standards for research during public health emergencies: distilling existing guidance to support COVID-19. *Ethical Stand Res Dur public Heal emergencies Distill Exist Guid to Support COVID-19 R&D*. 2020:1-4.

19. Sakthivel Sivam SM. Everything or Nothing - A Better Confidence Intervals for Binomial Proportion in Clinical Trial Data Analysis . Sakthivel Sivam , Quartesian LLC , Princeton , New Jersey Subbiah Meenakshisundaram , L . N Government College , Ponneri , India. 2016;(2014).

20. Mahase E. Covid-19: Two antibody tests are "highly specific" but vary in sensitivity, evaluations find. *BMJ*. 2020;369(May):m2066. doi:10.1136/bmj.m2066

21. Diggle PJ. Estimating Prevalence Using an Imperfect Test. *Epidemiol Res Int*. 2011;2011:1-5. doi:10.1155/2011/608719

22. COVID-19 Case Surveillance Public Use Data. https://covid.cdc.gov/covid-data-tracker/#national-lab.

23. https://www.jpost.com/israel-news/coronavirus-herd-immunity-not-in-israel-according-to-a-serological-study-630059.

24. Ibarrondo FJ, Fulcher JA, Goodman-Meza D, et al. Rapid Decay of Anti–SARS-CoV-2 Antibodies in Persons with Mild Covid-19. *N Engl J Med*. 2020:1-2. doi:10.1056/nejmc2025179

25. Bölke E, Matuschek C, Fischer JC. Loss of Anti–SARS-CoV-2 Antibodies in Mild Covid-19. *N Engl J Med*. 2020;383(17):1694-1698. doi:10.1056/nejmc2028468

26. Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel

coronavirus disease 2019. *Clin Infect Dis*. 2020;(M):2-3. doi:10.1093/cid/ciaa344

27. Wu LP, Wang NC, Chang YH, et al. Duration of antibody responses after severe acute respiratory syndrome. *Emerg Infect Dis*. 2007;13(10):1562-1564. doi:10.3201/eid1310.070576

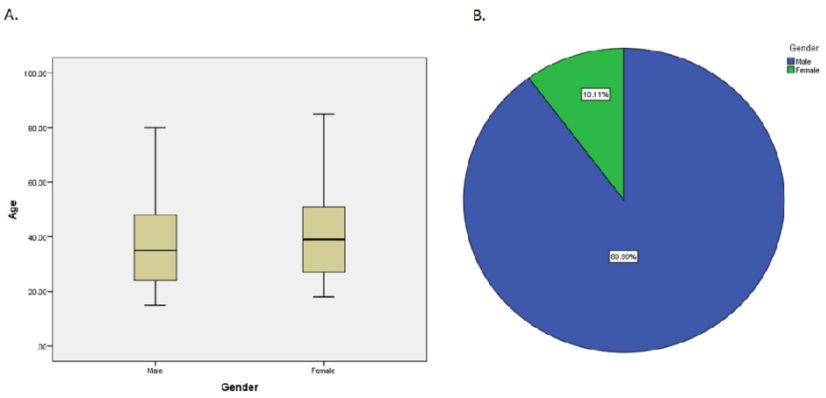

Figure 1
Caption : (a) Age and (b) gender distribution of the 1355 participants from Palestinian households in the West Bank. Blood samples were collected between 15th June 2020 and 30th June from the participants.

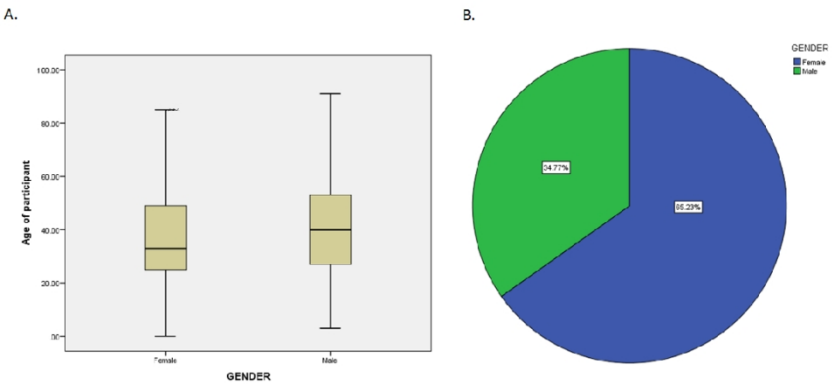

Figure 2
Caption : (a) Age and (b) Gender distribution of the 1136 participants visiting Medicare laboratories between the 1st May 2020 and 9th July 2020 for a routine checkup.

Supplementary Table 1: Governorates and localities included in the households sample

Governorate	Locality
Jenin	Sir
Jenin	Anza
Jenin	Al Araqa
Jenin	Al Mughayyir
Jenin	Al Fandaqumiya
Jenin	Al Judeida
Jenin	Ajja
Jenin	Birqin
Jenin	Meithalun
Jenin	Jaba
Jenin	Silat al Harithiya
Jenin	Arraba
Jenin	Yabad
Jenin	Al Yamun
Jenin	Qabatiya
Jenin	Jenin
Tubas	Ras al Faraa
Tubas	Aqqaba
Tubas	Tammun
Tubas	Tubas
Tulkarm	Kafa
Tulkarm	Kafr Jammal
Tulkarm	Kafr al Labad
Tulkarm	Nur Shams Camp
Tulkarm	Bala
Tulkarm	Tulkarm Camp
Tulkarm	Attil
Tulkarm	Tulkarm
Nablus	Iraq Burin
Nablus	Qusin
Nablus	As Sawiya
Nablus	Majdal Bani Fadil
Nablus	Sabastiya
Nablus	Ein Beit el Ma Camp
Nablus	Beit Dajan
Nablus	Qusra
Nablus	Askar Camp)al Qadeem(
Nablus	Awarta
Nablus	Asira ash Shamaliya
Nablus	Aqraba

Nablus	Beit Furik
Nablus	Balata Camp
Nablus	Nablus
Qalqiliya	Kafr Laqif
Qalqiliya	Jinsafut
Qalqiliya	Sanniriya
Qalqiliya	Azzun
Qalqiliya	Qalqiliya
Salfit	Deir Istiya
Salfit	Haris
Salfit	Biddya
Salfit	Salfit
Ramallah & Al-Bireh	Shabtin
Ramallah & Al-Bireh	Ein Arik
Ramallah & Al-Bireh	Beitin
Ramallah & Al-Bireh	Ein Yabrud
Ramallah & Al-Bireh	Arura
Ramallah & Al-Bireh	Beitillu
Ramallah & Al-Bireh	Deir Abu Mashaal
Ramallah & Al-Bireh	Khirbet Abu Falah
Ramallah & Al-Bireh	Beit Ur at Tahta
Ramallah & Al-Bireh	Shuqba
Ramallah & Al-Bireh	Qibya
Ramallah & Al-Bireh	Al Jalazun Camp
Ramallah & Al-Bireh	Beituniya
Ramallah & Al-Bireh	Ramallah
Ramallah & Al-Bireh	Al Bireh
Jericho & Al-Aghwar	Ein as Sultan Camp
Jericho & Al-Aghwar	Jericho)Ariha(
Jerusalem	Ash Sheikh Sad

Jerusalem	Beit Surik
Jerusalem	As Sawahira ash Sharqiya
Jerusalem	Hizma
Jerusalem	Qalandiya Camp
Jerusalem	Ar Ram & Dahiyat al Bareed
Jerusalem	Anata
Jerusalem	Al Eizariya
Bethlehem	Al Masara
Bethlehem	Wadi Rahhal
Bethlehem	Dar Salah
Bethlehem	Husan
Bethlehem	Hindaza and Bureidaa
Bethlehem	Nahhalin
Bethlehem	Ad Duheisha Camp
Bethlehem	Ad Doha
Bethlehem	Beit Sahur
Bethlehem	Beit Jala
Bethlehem	Beit Fajjar
Bethlehem	Bethlehem (Beit Lahm)
Hebron	An Najada
Hebron	Beit ar Rush al Fauqa
Hebron	Shuyukh al Arrub
Hebron	Al Burj and Al Bira
Hebron	Nuba
Hebron	Al Fawwar Camp
Hebron	Beit Kahil
Hebron	Kharas
Hebron	Beit Awwa
Hebron	Beit Ula
Hebron	Taffuh
Hebron	Beit Ummar
Hebron	Surif
Hebron	Tarqumiya
Hebron	Sair
Hebron	Bani Naim
Hebron	Idhna
Hebron	As Samu
Hebron	Halhul
Hebron	Adahiriya
Hebron	Dura
Hebron	Yatta

Hebron	Hebron (Al Khalil)

Supplementary Table 2: Governorates and localities included in the lab referrals sample

Governorate	Locality
Jericho	Jericho
Hebron	Dura
Hebron	Yatta
Hebron	Hebron (Al Khalil)
Hebron	Adahiriya
Bethany	Bethany
Bethlehem	Bethlehem
Jenin	Jenin
Ramallah	Ramallah
Ramallah	Silwad
Tubas	Tubas
Tulkarem	Tulkarem
Qalqiliah	Qalqiliah
Nablus	Nablus
Salfit	Bidia
Salfit	Salfit

Supplementary Table 3: Prevalence of symptoms reported by participants

Symptom	Yes N=1355	No N=1355	Don't Know N=1355
Fever	3.8%	95.4%	.8%
Sneezing	6.8%	92.4%	.8%
Dry Cough	5.7%	93.5%	.8%
Vomiting	1.1%	98.1%	.8%

Sore and red throat	4.3%	94.9%	.8%
Diarrhea	2.0%	97.2%	.8%
Muscle ache	3.2%	95.9%	.9%
Nasal Congestion	2.8%	96.3%	.8%
Skin rash or change in color of the thump or toe	1.2%	97.9%	.9%
Loss of sense of taste and smell	.7%	98.5%	.8%
Chest pain	1.7%	97.6%	.8%
Difficulty breathing	1.8%	97.4%	.8%
Loss of ability to speak or move	.6%	98.7%	.8%

Supplementary Table 4: Prevalence of chronic diseases reported by participants

Chronic Disease	Yes N=1355	No N=1355	Don't Know N=1355
Heart disease	5.1%	94.9%	0.0%

Blood pressure	11.9%	88.1%	0.0%
Cancer	.2%	99.8%	.0%
Kidney disease	.7%	99.2%	.1%
Nervous system disease	.7%	99.3%	0.0%
Diabetes	10.1%	89.9%	0.0%
Respiratory disease (Asthma)	4.4%	95.5%	.0%
Hospitalized through the past 6 months	4.2%	95.8%	.0%
On immunosuppressant drug?	1.2%	98.8%	0.0%

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Seroprevalence of SARS-CoV-2 the West Bank region of Palestine: a cross-sectional seroepidemiological study

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Seroprevalence of SARS-CoV-2 the West Bank region of Palestine: a cross-sectional seroepidemiological study

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Word count: 2853

Abstract

Objectives

Seroprevalence rates are important indicators to the epidemiology of COVID-19 and the extent of the pandemic given the existence of asymptomatic cases. The purpose of this study is to assess the seroprevalence rate in the Palestinian population residing in the West Bank.

Setting

The study involved 1355 participants from 11 governorates, including 112 localities in the West Bank and 1136 individuals visiting Palestinian medical laboratories.

Participants

Blood samples were collected between 15th June 2020 and 30th June 2020 from 1355 individuals from randomly selected households in the West Bank in addition to 1136 individuals visiting Palestinian medical laboratories between the 1st May 2020 and 9th July 2020 for a routine checkup.

Primary and secondary outcome measures

Out of the 2491 blood samples collected, serological tests for 2455 adequate serum samples were done using an Immunoassay for qualitative detection of antibodies against SARS-CoV-2. seroprevalence was estimated as the proportion of individuals who had a positive result in the total SARS-CoV-2 antibodies in the immunoassay

Results

The random sample of Palestinians living in the West Bank yielded 0% seroprevalence with 95% and an adjusted confidence interval [0, 0.0043], while the lab referrals sample yielded an estimated seroprevalence of 0.354% with 95% and an adjusted confidence interval [0.001325, 0.011566].

Conclusions

Our results indicate that as of mid-june 2020, seroprevalence in Palestine persist low and is inadequate to provide herd immunity, emphasizing the need to maintain health measures to keep the outbreak under control. Population-based seroprevalence studies are to be conducted periodically to monitor the SARS-CoV-2 seroprevalence in Palestine and inform policy makers about the efficacy of their surveillance system.

Strengths and limitations of this study

Strengths:

1- The random selection of household's residents collected between 15th June 2020 and 30th June 2020.

2- Good representation of females and children among the 1136 participants from Medicare laboratory referrals between 1st May 2020 and 9th July 2020.

Limitations:

1- Low representation in females represented in the random sample.

2- The random sample did not include children under the age of 15.

Introduction

Coronavirus disease 2019, known as COVID-19, is an infectious respiratory disease caused by novel coronavirus SARS-CoV-2 [1]. Since its emergence in Wuhan, China in December 2019 [2], SARS-CoV-2 has spread rapidly around the globe. A global pandemic was declared by the World Health Organization (WHO) [3,4] and new cases and deaths are being reported daily [5].

Most authorities rely on PCR testing results to estimate number of COVID-19 cases and make up-to-date decisions [6]. Thus, numbers of patients tested positive for SARS-CoV-2 through PCR testing, symptomatic patients, those admitted to hospitals, or deceased from COVID-19 are updated on a daily basis. However, the data may exclude a fraction of the population with previous mild or asymptomatic COVID-19 that has not been tested by PCR. The proportion of the

population who have overcome the infection without being noticed can probably be approximated by testing for antibodies against SARS-CoV-2. Antibodies may confer immunity to repeat infection and a high proportion of immune individuals can attenuate the epidemic. Measures of anti-SARS-CoV-2 seroprevalence can also be used to estimate the clinical impact of COVID-19. To this effect, several serological surveys of SARS-CoV-2 have been done worldwide [7–16].

Objective:

There is lack of data on the percentage of undiagnosed Palestinian population with previous mild or asymptomatic COVID-19. Prevalence of COVID-19 infections among Palestinians residing in the West Bank remains unknown and many are concerned about this uncertainty. To this end, we conducted a population cross sectional based seroepidemiological study to assess the spread of SARS-CoV-2 throughout the West Bank. The study included 2491 individuals, designed to be representative by cities (1355 from randomly selected households and 1136 from laboratory referrals). Elecsys® Anti-SARS-CoV-2 testing was done on 2455 adequate serum samples. Here, we describe the study design and the results of the first wave of the study.

Methods

Study design and participants

The study conducted is a cross-sectional serologic testing study aimed to investigate seropositivity for SARS-CoV-2 in the non-institutionalized Palestinian population residing in the West Bank.

The study involved 1355 participants from 11 governorates, including 112 localities (supplementary table 1). We used 3-stage cluster sampling to select 1395 households. The cluster of households or census track is considered to be a geographic location that is comprised of approximately 100 households. The process for conducting cluster sampling was carried as

follows: (1) Selecting a cluster of households, (2) Selecting 10 households randomly from each cluster and (3) Selecting a person at random from the selected household. The clusters were selected using probability proportional to size (PPS) sampling (Table 1).

Table 1: The PPS sampling algorithm

Location	# of households in the location	Cumulative
L1	X1	C1=X1
L2	X2	C2=X1+X2
L3	X3	C3=X1+X2+X3
.	.	.
.	.	.
.	.	.
Lk-1	Xk-1	Ck-1=X1+X2+…+Xk-1
Lk	Xk	Ck = X1+X2+…+Xk

To select the number of clusters within each population location: (1) we calculated the sampling interval which equals the total number of households divided by the total number of clusters need to be selected by the sample say for example (m). So, the sampling interval SI= N/m, where N is

the total number of households. (2) selected a random number R0 between 0 and SI. (3) calculated Ri as R0+i*SI, a cluster is selected in Li if Ri belongs to the interval [Ci-1, Ci].

Field work was carried out between 15th[th] June 2020 and 30[th] June 2020 by a team of registered nurses, laboratory technicians, nursing students and laboratory technician students from the Arab American University following standardized health protocols [17]. The random sample did not include children under the age of 15 and suffered from a low representation in females.

The study also included 1136 participants from Medicare® medical laboratories network referrals between 1[st] May 2020 and 9[th] July 2020 in 16 branches in the West Bank (supplementary table 2).

Participants donated a blood sample for antibodies detection. Blood samples were centrifuged and serum was separated, labelled, stored at -20C at AAUP laboratory until it was used.

Detection of antibodies

Serological tests for 2455 adequate serum samples were done using an Immunoassay for the qualitative detection of antibodies against SARS-CoV-2 (Elecsys® Anti-SARS-CoV-2**)** in human serum by using the Cobas analyzer cobas e 411 (Roche). The assay uses a recombinant protein representing the nucleocapsid (N) antigen for the determination of antibodies against SARS-CoV-2 with testing time of 18 minutes. The assay was reported to have a specificity of 100%, while the overall sensitivity was 83.87%, rising to 87.0% at 14 days after onset of symptoms, 87.7% 21 days after, and 100% more than 40 days after [18]. We included 6 samples from recovered cases with detected SARS-CoV-2 antibodies as a positive control.

Statistical Analysis

We estimated seroprevalence as the proportion of individuals who had a positive result in the total SARS-CoV-2 antibodies in the immunoassay.

We used Wilson Method With Continuity Correction and Boundary Truncation (WCCBT) to construct 95% CI for the population parameter of seroprevalence [19] .

We calculated the adjusted confidence of interval. Since the specificity of the kit used for the antibodies test is 100% and 83% respectively [18], we adjusted the confidence interval for seroprevalence according to the following transformation: Adjusted lower confidence limit= max[0, {a-(1-sp)}/(sp+se-1)] and adjusted upper confidence limit=min[1, {b-(1-sp)}/(sp+se-1)] [20]. The Low representation in females represented in the random sample required reweighting by gender. As for the Medicare Labs sample, the obtained estimates from the lab data are considered to be unbiased and did not require reweighting.

Patients and public involvement

The study involved 1355 participants from 11 governorates, including 112 localities and included 1136 participants from Medicare® laboratories referrals. The development of the research question and outcome measures was based on the public priorities to know the seroprevalence in the Palestinian community. Approval from National ethical committee was obtained (PHRC/HC/737/20). Written informed consent was obtained from the 1355 study participants and approvals were obtained from Medicare® laboratories for samples to be tested. Participants \ were notified of the results of the tests.

Results

Of the 1395 eligible individuals residing in households selected using 3-stage cluster sampling, 1355 participants agreed to participate in the study. The proportion of females was lower compared to males (137, 1218 respectively) including 349 in age group (15-24), 314 in age group (25-34), 377 in age group (35-49) and 315 in age group (50+). (Figure 1). The majority of the participants did not report having symptoms in the last three months nor prevailing chronic diseases (supplementary table 3 and 4). None of the tested specimens revealed presence of antibodies against SARS-CoV-2. A 95% CI for the population parameter of seroprevalence was [0.0, 0.0036]. A 95% CI for the population parameter of seroprevalence was [0.0, 0.0036], and an adjusted confidence interval of [0, 0.0043].

Of the1136 participants from Medicare laboratory referrals in 16 branches. The proportion of males was lower than females (395, 741 respectively) including 71 in age group lower less than 15, 173 in age group (15-24), 297 tests in age group (25-34), 290 in age group (35-49) and 305 in age group (50+) (Figure 2). Records of symptoms and chronic diseases were unattainable. Out of the 1136 tested participants, 3 males, ages 38, 58, 59 and 1 female, age 40 revealed antibodies against SARS-CoV-2, with 95% CI [0.0011,0.0096] and an adjusted confidence interval of [0.001325, 0.011566].

All serum samples were adequate for testing. Out of the 1136 tested participants, 4 revealed antibodies against Sars-CoV-2 with 95% CI [0.0011,0096].

Discussion

To our knowledge, this is the first SARS-CoV-2 seroprevalence study in the Palestine. The findings from this seroprevalence study for SARS-CoV-2 indicate that the estimated

seroprevalence of the total SARS-CoV-2 antibodies persist low as of mid of June. The random sample of Palestinians living in the West Bank yielded 0% seroprevalence with 95% and an adjusted confidence interval of [0, 0.0043], while the lab referrals sample yielded an estimated seroprevalence of 0.354% with 95% and an adjusted confidence [0.001325, 0.011566].

The low SARS-CoV-2 antibody prevalence in our population can be explained by the imposed total lockdown in the first three months when cases were under control and only reached around 800 cases by May. Our sampling dates ranged from 15th June 2020-30th June 2020 in the random sample and between 1st May 2020 and 9th July 2020 in the lab referrals sample. The GoP extended the state of emergency and imposed total lockdown in the first three months. The samples were collected after this strict lockdown which was accompanied by a drop in disease prevalence. Covid-19 cases were under control. The reported cases by the Palestinian ministry of health at the beginning of the data collection process by mid-June was 689 cases, and the reported cases rose to 2765 cases by the end of June [21]. However, it takes 10-14 days for antibodies against SARS-CoV-2 to go up, therefore, our results indeed reflect the situation by mid of June. Also, It was previously reported that antibodies against SARS-CoV-2 may drop or even disappear in patients with mild Covid-19 [22–24] which may have led to the inability to detect antibodies in a few previously positive cases.

Seroprevalence in Palestine is very close to that identified in Jordan (0% prevalence) [15], a neighboring country, which was explained to be due to the strict closures implemented by the Jordanian government and the eventual curtailing of infections in Jordan. Also, Seroprevalence in Maine and Montana was 0.4% and 0.5% respectively by end of August 2020 [25]. In comparison to other countries like Spain, Italy. Japan India, Los Angeles, Germany, Switzerland the seroprevalence in Palestine is low [7–16]. Similarly, the seroprevalence among Palestinians residing in the West Bank was shown to be lower than that in Israel as reported in the first conducted

serological study of 1,700 tests. The study suggested that 2.5 percent of the Israeli population, have had the coronavirus[26]. It is, however, noteworthy that a comparison with other countries may be problematic due to the timing and the stage of the pandemic which may vary affecting the seroprevalence estimates.

A key strength of our study is the random selection of household's residents collected between 15th June 2020 and 30th June 2020. The clusters were selected using probability proportional to size (PPS) sampling. This technique ensures getting self-weighting sample which can be used to produce unbiased estimators for the parameters of interest. The sample was supposed to be stratified by gender and age. However, the female response was low and samples from females were more difficult to obtain due to a cultural boundary. In fact, women were less open to welcoming a team of nurses at home for research purposes. Also, the random sample did not include children under the age of 15 to avoid anxiety due to fear of needles in the study to eliminate personal fears due to blood withdrawal. To ensure that the estimated prevalence in the random sample was unbiased, we reweighted the sample by gender. Except for cultural issues resulting in the low response rate from women in the random sample, we do not believe there were any issues that would lead participants to opt out from the study.

As for the lab referrals sample, it represents the population of the lab referrals between the 1st May 2020 and 9th July 2020. The seroprevalence in this sample was 4 positive cases out of the 1136 samples tested. Since the seroprevalence within the lab referral population is close to zero, we used Wilson Method with Continuity Correction and Truncation (WCCBT) to construct a 95% confidence interval for the population parameter of seroprevalence [0.0011,0096]. In comparison to household samples that were collected between 15th-30th of June, laboratory referral samples include a good representation of females and children below the age of 15 (Figure 2). Also, samples

were collected starting from May 1st, which may better represent the small peaks of SARS-CoV-2 reported cases in Palestine and thus explain the presence of few positive samples in comparison to null in household samples. The sample was randomly selected by the lab data managers. Although females were not represented among the1355 adults from Palestinian households in the, they were represented among the 1136 individuals visiting laboratories; out of the 1136, 741, more than 50% of the participants were females (Figure 2). Hence, the obtained estimates from the lab data are considered to be unbiased.

Our study only detected SARS-CoV-2 antibodies. It was previously reported that antibodies against SARS-CoV-2 may drop or even disappear in patients with mild Covid-19, which may have led to the inability to detect antibodies in a few previously positive cases [23],[22] . Also, it is important to recognize that cellular immunity may play a role in providing immunity against SARS-CoV-2 reinfection[18]. Further studies aimed at testing cellular immunity are important. It is also noteworthy that previous studies have indicated that asymptomatic individuals were reported to have a weaker immune response to SARS-CoV-2 infection and a higher percentage of asymptomatic individuals became seronegative when compared to symptomatic individuals in the early recovering phases. The reduction in neutralizing antibody levels may have implications for immunity strategy and serological surveys [24,27].

In conclusion, our study provides estimates of SARS-CoV-2 seroprevalence in Palestine. Our results reflect the seroprevalence as of mid of June. It is noteworthy that on May 25th, the government of Palestine eased the restrictions following a decline in cases which led to a surge in cases beginning of July, with the epicenter of the epidemic in Hebron accounting for over 70 % of active cases implying a possible increase in seroprevalence after July. Reported cases rose to 2765 cases by the end of June. By December 2020, the cumulative number of positive cases grew to

150,046 cases [21] . In this situation, health measures have to be taken to keep the outbreak under control. In order to monitor the SARS-CoV-2 seroprevalence in Palestine and inform policy makers about the efficacy of their surveillance system. With the surge in cases, conducting population-based seroprevalence studies on a regular basis is important.

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Conflict of Interest Disclosures

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Authors contribution

Research design: Nouar Qutob, Zaidoun Salah, Faisal Awartani

Field work coordination: Mohammad Asia, Imad Abu Khader

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Manuscript revisions: Nouar Qutob, Faisal Awartani, Zaidoun Salah

Methodology and lab work: Nouar Qutob, Khaled Herzallah, Nadeen Balqis, Husam Sallam

Data sharing

Data are available upon reasonable request

Figure Legends

Figure 1: (a) Age and (b) gender distribution of the 1355 participants from Palestinian households in the West Bank. Blood samples were collected between 15th June 2020 and 30th June from the participants.

Figure 2: (a) Age and (b) Gender distribution of the 1136 participants visiting Medicare laboratories between the 1st May 2020 and 9th July 2020 for a routine checkup.

References

1. Mayo clinic. oronavirus disease 2019 (COVID-19).

2. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *J Med Virol*. 2020;92(4):401-402. doi:10.1002/jmv.25678

3. World Health Organization. *Novel Coronavirus(2019-NCoV), Situation Report - 12*.; 2020.

4. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health — The latest 2019 novel coronavirus outbreak in Wuhan, China The. 2020;(January).

5. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU).

6. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA - J Am Med Assoc*. 2020;2019:2019-2020. doi:10.1001/jama.2020.4683

7. Snoeck CJ, Vaillant M, Abdelrahman T, et al. Prevalence of SARS-CoV-2 infection in the Luxembourgish population the CON-VINCE study. *Medrxiv*. 2020:2020.05.11.20092916. doi:10.1101/2020.05.11.20092916

8. Wu X, Fu B, Chen L, Feng Y. Serological tests facilitate identification of asymptomatic SARS-CoV-2 infection in Wuhan, China. *J Med Virol*. 2020:2-3. doi:10.1002/jmv.25904

9. Bryan A, Pepper G, Wener MH, et al. Performance Characteristics of the Abbott Architect SARS-CoV-2 IgG Assay and Seroprevalence in Boise, Idaho. *J Clin Microbiol*. 2020;(May). doi:10.1128/JCM.00941-20

10. Stringhini S, Wisniak A, Piumatti G, et al. Repeated seroprevalence of anti-SARS-CoV-2 IgG antibodies in a population-based sample from Geneva, Switzerland. *medRxiv*. 2020:2020.05.02.20088898. doi:10.1101/2020.05.02.20088898

11. Valenti L, Bergna A, Pelusi S, et al. SARS-CoV-2 seroprevalence trends in healthy blood donors during the COVID-19 Milan outbreak. *medRxiv*. 2020:2020.05.11.20098442. doi:10.1101/2020.05.11.20098442

12. Shakiba M, Hashemi Nazari SS, Mehrabian F, Rezvani SM, Ghasempour Z, Heidarzadeh A. Seroprevalence of COVID-19 virus infection in Guilan province, Iran. *medRxiv*. 2020:2020.04.26.20079244. doi:10.1101/2020.04.26.20079244

13. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet (London, England)*. 2020;6736(20):1-11. doi:10.1016/S0140-6736(20)31483-5

14. Stadlbauer D, Amanat F, Chromikova V, et al. SARS-CoV-2 Seroconversion in Humans: A Detailed Protocol for a Serological Assay, Antigen Production, and Test Setup. *Curr Protoc Microbiol*. 2020;57(1):2425-2427. doi:10.1002/cpmc.100

15. Sughayer MA, Mansour A, Nuirat A Al, Souan L, Ghanem M, Siag M. Covid-19 Seroprevalence rate in healthy blood donors from a community under strict lockdown measures. *medRxiv*. 2020:2020.06.06.20123919. doi:10.1101/2020.06.06.20123919

16. Hains DS, Schwaderer AL, Carroll AE, Starr MC, Wilson AC. Seroprevalence of SARS-CoV-2 – Specific Antibodies Among Adults in Los Angeles County , California , on April 10-11 , 2020. 2020;323(23):2425-2427. doi:10.1002/cpmc.100

17. World Health Organization. Ethical standards for research during public health emergencies: distilling existing guidance to support COVID-19. *Ethical Stand Res Dur public Heal emergencies Distill Exist Guid to Support COVID-19 R&D*. 2020:1-4.

18. Mahase E. Covid-19: Two antibody tests are “highly specific” but vary in sensitivity, evaluations find. *BMJ*. 2020;369(May):m2066. doi:10.1136/bmj.m2066

19. Sakthivel Sivam SM. Everything or Nothing - A Better Confidence Intervals for Binomial Proportion in Clinical Trial Data Analysis . Sakthivel Sivam , Quartesian LLC , Princeton , New Jersey Subbiah Meenakshisundaram , L . N Government College , Ponneri , India. 2016;(2014).

20. Diggle PJ. Estimating Prevalence Using an Imperfect Test. *Epidemiol Res Int*. 2011;2011:1-5. doi:10.1155/2011/608719

21. https://corona.ps/.

22. Bölke E, Matuschek C, Fischer JC. Loss of Anti–SARS-CoV-2 Antibodies in Mild Covid-19. *N Engl J Med*. 2020;383(17):1694-1698. doi:10.1056/nejmc2028468

23. Ibarrondo FJ, Fulcher JA, Goodman-Meza D, et al. Rapid Decay of Anti–SARS-CoV-2 Antibodies in Persons with Mild Covid-19. *N Engl J Med*. 2020:1-2. doi:10.1056/nejmc2025179

24. Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis*. 2020;(M):2-3. doi:10.1093/cid/ciaa344

25. COVID-19 Case Surveillance Public Use Data. https://covid.cdc.gov/covid-data-tracker/#national-lab.

26. https://www.jpost.com/israel-news/coronavirus-herd-immunity-not-in-israel-according-to-a-serological-study-630059.

27. Wu LP, Wang NC, Chang YH, et al. Duration of antibody responses after severe acute respiratory syndrome. *Emerg Infect Dis*. 2007;13(10):1562-1564. doi:10.3201/eid1310.070576

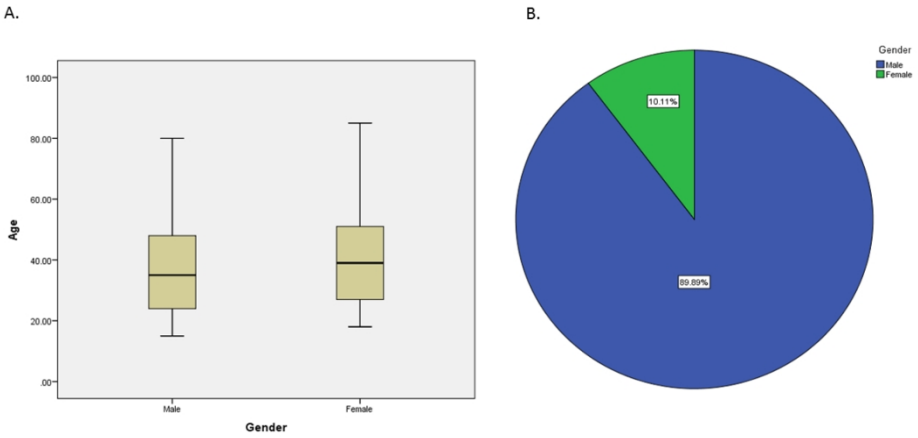

Figure 1: (a) Age and (b) gender distribution of the 1355 participants from Palestinian households in the West Bank. Blood samples were collected between 15th June 2020 and 30th June from the participants.

338x190mm (96 x 96 DPI)

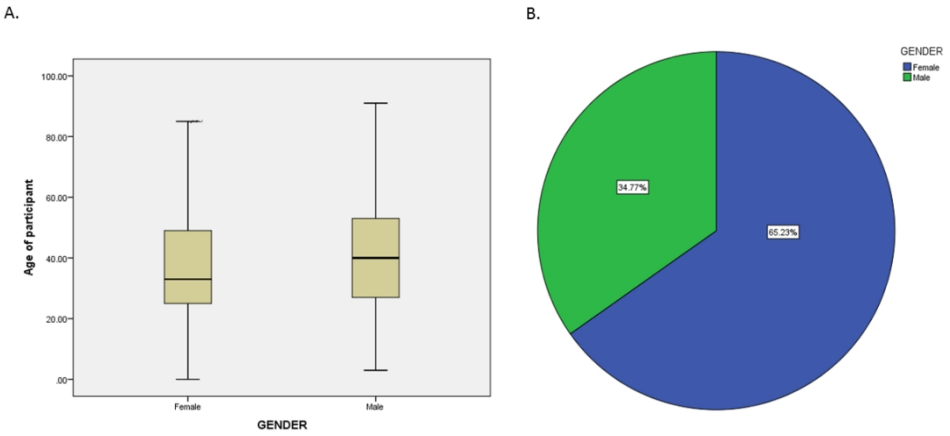

Figure 2: (a) Age and (b) Gender distribution of the 1136 participants visiting Medicare laboratories between the 1st May 2020 and 9th July 2020 for a routine checkup.

338x190mm (96 x 96 DPI)

Supplementary Table 1: Governorates and localities included in the households sample

Governorate	Locality
Jenin	Sir
Jenin	Anza
Jenin	Al Araqa
Jenin	Al Mughayyir
Jenin	Al Fandaqumiya
Jenin	Al Judeida
Jenin	Ajja
Jenin	Birqin
Jenin	Meithalun
Jenin	Jaba
Jenin	Silat al Harithiya
Jenin	Arraba
Jenin	Yabad
Jenin	Al Yamun
Jenin	Qabatiya
Jenin	Jenin
Tubas	Ras al Faraa
Tubas	Aqqaba
Tubas	Tammun
Tubas	Tubas
Tulkarm	Kafa
Tulkarm	Kafr Jammal
Tulkarm	Kafr al Labad
Tulkarm	Nur Shams Camp
Tulkarm	Bala
Tulkarm	Tulkarm Camp
Tulkarm	Attil
Tulkarm	Tulkarm
Nablus	Iraq Burin
Nablus	Qusin
Nablus	As Sawiya
Nablus	Majdal Bani Fadil
Nablus	Sabastiya
Nablus	Ein Beit el Ma Camp
Nablus	Beit Dajan
Nablus	Qusra
Nablus	Askar Camp)al Qadeem(
Nablus	Awarta
Nablus	Asira ash Shamaliya
Nablus	Aqraba

Nablus	Beit Furik
Nablus	Balata Camp
Nablus	Nablus
Qalqiliya	Kafr Laqif
Qalqiliya	Jinsafut
Qalqiliya	Sanniriya
Qalqiliya	Azzun
Qalqiliya	Qalqiliya
Salfit	Deir Istiya
Salfit	Haris
Salfit	Biddya
Salfit	Salfit
Ramallah & Al-Bireh	Shabtin
Ramallah & Al-Bireh	Ein Arik
Ramallah & Al-Bireh	Beitin
Ramallah & Al-Bireh	Ein Yabrud
Ramallah & Al-Bireh	Arura
Ramallah & Al-Bireh	Beitillu
Ramallah & Al-Bireh	Deir Abu Mashaal
Ramallah & Al-Bireh	Khirbet Abu Falah
Ramallah & Al-Bireh	Beit Ur at Tahta
Ramallah & Al-Bireh	Shuqba
Ramallah & Al-Bireh	Qibya
Ramallah & Al-Bireh	Al Jalazun Camp
Ramallah & Al-Bireh	Beituniya
Ramallah & Al-Bireh	Ramallah
Ramallah & Al-Bireh	Al Bireh
Jericho & Al-Aghwar	Ein as Sultan Camp
Jericho & Al-Aghwar	Jericho)Ariha(
Jerusalem	Ash Sheikh Sad

Jerusalem	Beit Surik
Jerusalem	As Sawahira ash Sharqiya
Jerusalem	Hizma
Jerusalem	Qalandiya Camp
Jerusalem	Ar Ram & Dahiyat al Bareed
Jerusalem	Anata
Jerusalem	Al Eizariya
Bethlehem	Al Masara
Bethlehem	Wadi Rahhal
Bethlehem	Dar Salah
Bethlehem	Husan
Bethlehem	Hindaza and Bureidaa
Bethlehem	Nahhalin
Bethlehem	Ad Duheisha Camp
Bethlehem	Ad Doha
Bethlehem	Beit Sahur
Bethlehem	Beit Jala
Bethlehem	Beit Fajjar
Bethlehem	Bethlehem (Beit Lahm)
Hebron	An Najada
Hebron	Beit ar Rush al Fauqa
Hebron	Shuyukh al Arrub
Hebron	Al Burj and Al Bira
Hebron	Nuba
Hebron	Al Fawwar Camp
Hebron	Beit Kahil
Hebron	Kharas
Hebron	Beit Awwa
Hebron	Beit Ula
Hebron	Taffuh
Hebron	Beit Ummar
Hebron	Surif
Hebron	Tarqumiya
Hebron	Sair
Hebron	Bani Naim
Hebron	Idhna
Hebron	As Samu
Hebron	Halhul
Hebron	Adahiriya
Hebron	Dura
Hebron	Yatta

Hebron	Hebron (Al Khalil)

Supplementary Table 2: Governorates and localities included in the lab referrals sample

Governorate	Locality
Jericho	Jericho
Hebron	Dura
Hebron	Yatta
Hebron	Hebron (Al Khalil)
Hebron	Adahiriya
Bethany	Bethany
Bethlehem	Bethlehem
Jenin	Jenin
Ramallah	Ramallah
Ramallah	Silwad
Tubas	Tubas
Tulkarem	Tulkarem
Qalqiliah	Qalqiliah
Nablus	Nablus
Salfit	Bidia
Salfit	Salfit

Supplementary Table 3: Prevalence of symptoms reported by participants

Symptom	Yes N=1355	No N=1355	Don't Know N=1355
Fever	3.8%	95.4%	.8%
Sneezing	6.8%	92.4%	.8%
Dry Cough	5.7%	93.5%	.8%
Vomiting	1.1%	98.1%	.8%

Sore and red throat	4.3%	94.9%	.8%
Diarrhea	2.0%	97.2%	.8%
Muscle ache	3.2%	95.9%	.9%
Nasal Congestion	2.8%	96.3%	.8%
Skin rash or change in color of the thump or toe	1.2%	97.9%	.9%
Loss of sense of taste and smell	.7%	98.5%	.8%
Chest pain	1.7%	97.6%	.8%
Difficulty breathing	1.8%	97.4%	.8%
Loss of ability to speak or move	.6%	98.7%	.8%

Supplementary Table 4: Prevalence of chronic diseases reported by participants

Chronic Disease	Yes N=1355	No N=1355	Don't Know N=1355
Heart disease	5.1%	94.9%	0.0%

Blood pressure	11.9%	88.1%	0.0%
Cancer	.2%	99.8%	.0%
Kidney disease	.7%	99.2%	.1%
Nervous system disease	.7%	99.3%	0.0%
Diabetes	10.1%	89.9%	0.0%
Respiratory disease (Asthma)	4.4%	95.5%	.0%
Hospitalized through the past 6 months	4.2%	95.8%	.0%
On immunosuppressant drug?	1.2%	98.8%	0.0%

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.