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Viral Analysis of Acute SARS-CoV-2 Infections in the prospective COVID-19 Cohort, Munich (KoCo19)

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Table 1: Abbreviations

COVID-19	Coronavirus Disease 2019
CT-value	Cycle threshold value
DIDTM	Division of Infectious Diseases and Tropical Medicine
DNA	Deoxyribonucleic acid
KoCo19	Prospektive COVID-19 Kohorte München/ Prospective COVID-19 cohort Munich
PCR	Polymerase Chain Reaction
RT-PCR	Reverse transcriptase Polymerase Chain Reaction
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
STT	Symptom To Test Time

List of publications

* Publication I and II are part of the cumulative thesis.

Publication I*

Michael Pritsch, Katja Radon, Abhishek Bakuli, Ronan Le Gleut, Laura Olbrich, Jessica Michelle Guggenbühl Noller, Elmar Saathoff, Noemi Castelletti, Mercè Garí, Peter Pütz, Yannik Schälte, Turid Frahnow, Roman Wölfel, Camilla Rothe, Michel Pletschette, Dafni Metaxa, Felix Forster, Verena Thiel, Friedrich Rieß, Maximilian Nikolaus Diefenbach, Günter Fröschl, Jan Bruger, Simon Winter, Jonathan Frese, Kerstin Puchinger, Isabel Brand, Inge Kroidl, Jan Hasenauer, Christiane Fuchs, Andreas Wieser, Michael Hoelscher, and on behalf of the KoCo19 study group. *Prevalence and Risk Factors of Infection in the Representative COVID-19 Cohort Munich;* Int J Environ Res Public Health. 2021 March 30; 18(7):3572. doi: 10.3390/ijerph18073572

Publication II*

Kerstin Puchinger, Castelletti Noemi, Raquel Rubio-Acero, Christof Geldmacher, Tabea M. Eser, Flora Deák, Ivana Paunovic, Abhishek Bakuli, Elmar Saathoff, Alexander von Meyer, Alisa Markgraf, Philline Falk, Jakob Reich, Friedrich Riess, Philipp Girl, Katharina Müller, Katja Radon, Jessica Michelle Guggenbuehl Noller, Roman Wölfel, Michael Hoelscher, Inge Kroidl, Andreas Wieser, Laura Olbrich *The interplay of viral loads, clinical presentation, and serological responses in SARS-CoV-2 – Results from a prospective cohort of outpatient COVID-19 cases;* Virology. 2022 Apr; 569: 37–43. Published online 2022 Feb 18. doi: 10.1016/j.virol.2022.02.002

Publication III

Kami Pekayvaz, Alexander Leunig, Rainer Kaiser, Markus Joppich, Sophia Brambs, Aleksandar Janjic, Oliver Popp, Daniel Nixdorf, Valeria Fumagalli, Nora Schmidt, Vivien Polewka, Afra Anjum, Viktoria Knottenberg, Luke Eivers, Lucas E. Wange, Christoph Gold, Marieluise Kirchner, Maximilian Muenchhoff, Johannes C. Hellmuth, Clemens Scherer, Raquel Rubio Acero, Tabea Eser, Flora Deák, Kerstin Puchinger, Niklas Kuhl, Andreas Linder, Kathrin Saar, Lukas Tomas, Christian Schulz, Andreas

Wieser, Wolfgang Enard, Inge Kroidl, Christof Geldmacher, Michael von Bergwelt-Baildon, Oliver T. Keppler, Mathias Munschauer, Matteo Iannacone, Ralf Zimmer, Philipp Mertins, Norbert Hubner, Michael Hoelscher, Steffen Massberg, Konstantin Stark, Leo Nicola, *Protective immune trajectories in early viral containment of non-pneumonic SARS-CoV-2 infection*; Nat Commun. 2022 Feb 23;13(1):1018. *doi: 10.1038/s41467-022-28508-0*

Publication IV

Katja Radon, Abhishek Bakuli, Peter Pütz, Ronan Le Gleut, Jessica Michelle Guggenbuehl Noller, Laura Olbrich, Elmar Saathoff, Mercè Garí, Yannik Schälte, Turid Frahnow, Roman Wölfel, Michael Pritsch, Camilla Rothe, Michel Pletschette, Raquel Rubio-Acero, Jessica Beyerl, Dafni Metaxa, Felix Forster, Verena Thiel, Noemi Castelletti, Friedrich Rieß, Maximilian N. Diefenbach, Günter Fröschl, Jan Bruger, Simon Winter, Jonathan Frese, Kerstin Puchinger, Isabel Brand, Inge Kroidl, Andreas Wieser, Michael Hoelscher, Jan Hasenauer, Christiane Fuchs, *From first to second wave: follow-up of the prospective COVID-19 cohort (KoCo19) in Munich (Germany);* BMC Infect Dis. 2021 Sep 8;21(1):925. *doi: 10.1186/s12879-021-06589-4*

Publication V

Tabea M. Eser, Olga Baranov, Manuel Huth, Mohamed I. M. Ahmed, Flora Deák, Kathrin Held, Luming Lin, Kami Perkayvaz, Alexander Leuning, Leo Nicolai, Georgios Pollakis, Marcus Buggert, David A. Price, Raquel Rubio-Acero, Jakob Reich, Philine Falk, Alisa Markgraf, Kerstin Puchinger, Noemi Castelletti, Laura Olbrich, Kanika Vanshylla, Florian Klein, Andreas Wieser, Jan Hasenauer, Inge Kroidl, Michael Hölscher, Christof Geldmacher, *Early nucleocapsid-specific T cell responses associate with control of SARS-CoV-2 in the upper airways and reduced systemic inflammation before seroconversion. Preprint:* https://doi.org/10.21203/rs.3.rs-2222184/v1; accepted for publication in Nature Communications

1. Contribution to the publications

1.1. Contribution to Publication I

Since April 2020, when study activities were prepared, I was part of the KoCo19 study team, mainly responsible for clinical activities. In this capacity, I regularly performed households-visits to recruit participants and perform all study-related activities. I was involved in organizing and executing the operational aspects of the main-study, including: scheduling the participants appointments, organizing study teams, obtaining informed consent, collecting and reporting the RT-PCR swab test results, sampling of blood. I was also involved in designing and disseminating the standard operating procedures (SOP) on the collection and documentation of swab-instructions for the fieldworkers and a short video clip for self-testing using of fingerstick blood for the participants as part of the main study [42]. Due to my contributions in the organization, management, and acquisition of data as a fieldworker and doctoral candidate I am listed as a co-author in the epidemiological paper “Prevalence and Risk Factors of Infection in the Representative COVID-19 Cohort Munich”. This work was published March 30th 2021 in the International Journal of Environmental Research and Public Health [41].

1.2. Contribution to Publication II

My thesis focussed on the description of viral data, such as viral shedding over time and viral loads during the course of a SARS-CoV-2 infection, and the correlation of these with serological responses and clinical presentation.

First and foremost, I contributed to formulating the research questions and executing the analyses outlined above in KoCo19-Immu, jointly with my supervisors PD Dr Inge Kroidl and Dr Laura Olbrich and Dr Noemi Castelletti, DIDTM’s senior statistician. Operationally, I was part of the fieldworker teams conducting the household visits, where participants were informed of all the relevant information pertaining to the study. Similar to the KoCo-19 main study, we collected blood samples and swaps of the participants, who were regularly followed-up at defined timepoints for the performance of antibody analysis, viral quantification, and viral culture (table 3).

Table 3: Protocol defined timepoints.

Examination	**Week 0**	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Week 8**	**Week 26 (+/-14d)**	**Week 52 (+/-14d)**
Blood samples:		X	X	X	X	X	X	X
Respiratory samples:								
Viral quantification	X	X		X	X	X	X	X
Viral culture		X		X	X	X		

In addition, I contributed to the development of the web-based symptom questionnaires, and conducted phone interviews for those participants who were unable to complete the online form. Aside from the clinical work and the collection of data in the first year of the study, I analysed the data with the open source software R-studio (Version R 4.0.3). The statistical analysis was corrected and supplemented by Dr Noemi Castelletti. Thus, first authorship of the manuscript "The interplay of viral loads, clinical presentation, and serological responses in SARS-CoV-2 – Results from a prospective cohort of outpatient COVID-19 cases" was shared. I wrote the manuscript with the help of Dr Noemi Castelletti during the year 2021 and submitted it in December 2021. It was corrected by my supervisors PD Dr Inge Kroidl, Dr Laura Olbrich and PD Dr Andreas Wieser. It was accepted for publication February 15th, 2022, in Virology.

2. Introduction

Towards the end of 2019, the first clusters of pneumonia of an unknown primary in the province of Wuhan in China were reported [1, 2]. By January 2020, 41 pneumonia cases were described and later identified and characterized as SARS-CoV-2 infections (Severe Acute Respiratory Syndrome Coronavirus 2) [1]. Due to international travel activities, the virus was enabled to spread worldwide within a short period of time – the first case outside of China was reported in Thailand in mid-January 2020 [2]. On January 27th, 2020, the first SARS-CoV-2 infection in Germany was confirmed at the Division of Infectious Diseases and Tropical Medicine Munich, Ludwig Maximilians University Hospital (DIDTM) [3]. On January 30th, the WHO proclaimed the outbreak of SARS-CoV-2 as a public health emergency of international concern [1, 2]. Following this, in February 2020, the WHO announced COVID-19 (Coronavirus Disease 2019) as the name for the new disease induced by SARS-CoV-2 infection [1].

The seasonal growth of SARS-CoV-2 cases is described in 'waves' [4]; the first German wave started in February 2020 and ended in April 2020. September 2020 marked the beginning of the second wave in Germany due to the increasing number of infections, with the third wave occurring during the spring of 2021 [5]. The 'incidence rate' describes the quantity of new cases emerging within a population during a specific time period [6]. The German government used the incidence rate as the main indicator to monitor and adjust infection preventative measures, which averaged over a seven-day period. The reproduction number (R) is a unit of measure which expresses the average number of people who become infected due to transmission from a single SARS-CoV-2 positive individual [6].

2.1. Aetiology and pathogenesis

Seven human pathogenic coronavirus-species have been described so far: two types of alphacoronavirus including HCoV-NL63 and HCoV-229E, and five types of betacoronavirus (**SARS-CoV-2,** SARS-CoV, MERS-CoV, HCoV-HKU1, HCoV-OC43) [6, 7]. Several of these cause common colds, especially within certain groups, including children in their early childhood and the elderly; furthermore, those who are immunosuppressed are at risk of severe pneumonia [7].

2.1.1. SARS-CoV-2

SARS-CoV-2, is a membrane-enveloped RNA-virus with a diameter of 80-140nm and possesses a single-stranded RNA-genome with positive polarity, encoding for several non-structural and for the four structural proteins forming the viral membrane (explained further in chapter 4.2. SARS-CoV-2) [8]. This betacoronavirus expresses spike proteins on the surface, those spike proteins are responsible for entering the host cell and have two subunits: the S1 and the S2. The receptor-binding domain (RBD) is considered to be part of the S1-subunit, its function is to bind the host cell receptor [9]. The S2-subunit allows the viral envelope to fuse with the membrane of the cell [9]. The spike proteins induce neutralizing antibodies, which are fundamental for the immune response and consequently for the development of vaccinations [10]. Homologous recombination allows the coronavirus to expand its economic spectrum [7, 11].

Since the beginning of the circulation of SARS-CoV-2 in humans, multiple mutations have been documented, as the virus envelops polymorphous nucleotide positions in different reading frames in the viral genome (as for example: RDRP, S, ORF3A, ORF8, N) [12]. During the time of the KoCo19-Immu study, which is the basis of this thesis and was conducted from May to December 2020, wild type SARS-CoV-2 was the predominant variant [13].

SARS-CoV-2 virulence and infectivity are determined by its molecular structure and function [14, 15]. Different mutations of the surface proteins can lead to higher pathogenicity and infectivity [14]. There are several structural proteins, among them spike (S), membrane (M), envelope (E), and nucleocapsid (N): figure 1 provides a schematic overview on the viral surface.

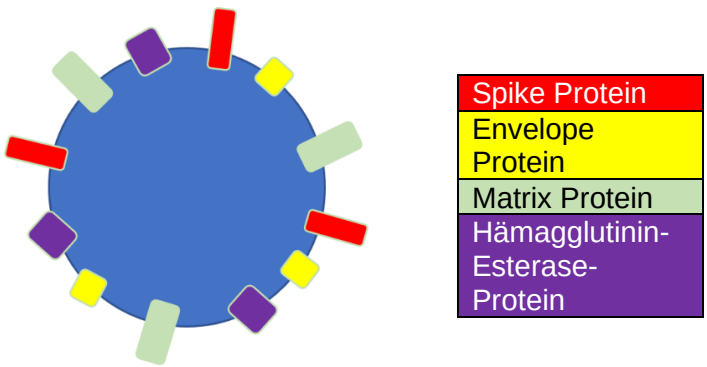

Figure 1: Modified after "Novel 2019 coronavirus structure, mechanism of action, antiviral drug promises and rule out against its treatment" [29]

Many viral processes, such as entering the host cell or formation of the virus particle, are dependent on these proteins [16, 17].

In addition to structural proteins, there are also different non-structural proteins, which are responsible for a large number of functions of SARS-CoV-2. For example, orf1ab and orf1a are expressed in the virus transformation phase producing two large polyproteins called pp1ab and pp1a. These two are then cleaved into 16Nsps participating in many viral processes as replication and transcription [16, 17].

2.1.2. The mechanism of SARS-CoV-2 infection

The interaction between the viral spike protein S and the membrane bound aminopeptidase (ACE2) on the host cell mediated via dipeptidyl peptidase-4 are fundamental for the entering process of SARS-CoV-2 [17]. ACE-2 is a type I transmembrane metallocarboxypeptidase expressed in many different types of tissues, both upper and lower respiratory tract as well as myocardium and gastrointestinal tract, which are crucial for understanding why the virus affects different tissues. The function of ACE-2 in the human body is not fully understood and explored yet, but it is assumed that it plays an important role in cardiac function [18, 19].

The virus enters the host cell cytosol by TMPRSS2, standing for transmembrane protease serine 2 [16]. After the virus enters the host cell, the viral multiplication cycle begins: first, in the phase of uncoating, nucleic acid from the endosome is released into the cytosol [16]. Subsequently, translation of the viral gene, replication and transcription follow [16]. Once the viral multiplication cycle has ended, the assembly phase begins, during which different viral components are combined. The life circle of the SARS-CoV-2 ends with the exocytosis and the invasion of more cells [16].

2.2. Clinical presentation

COVID-19 is a multifaceted disease that manifests primarily in organs that exhibit high levels of the ACE-2 receptor, which enables SARS-CoV-2 to invade the cell [20]. The lung is an organ frequently affected by SARS-CoV-2. An infection with SARS-CoV-2 often progresses to pneumonia, which in turn can progress to ARDS (Acute Respiratory Distress Syndrome) necessitating intensive care [21]. Neurologic symptoms are also common during SARS-CoV-2 infection. Patients often suffer from

headache, hyposmia and anosmia, vertigo, and mental confusion [22]. Nausea, vomiting, diarrhoea and abdominal pain are the most common gastrointestinal symptoms [23].

Damage of kidney, heart and other organs were more likely in severe cases with the need of intensive medical care [24, 25]. In 7 to 17% of patients with moderate disease, high levels of the cardiac enzyme troponin were measured as a sign of myocardial damage [25, 26]. Among those, approximately 22 to 31% needed further intensive medical care, including the treatment of myocarditis, myocardial infarction, heart failure or thromboembolic events [27].

The following table summarizes the most common symptoms during a SARS-CoV-2 infection in Germany according to RKI: [6]

Table 2: The five most common symptoms during a SARS-CoV-2 infection in Germany (February 2022).

Symptom	Prevalence (%)
Cough	42%
Cold	31%
Fever	26%
Loss of taste/ Loss of smell	19%
Pneumonia	1%

2.3. Diagnostic approaches for SARS-CoV-2 infection

2.3.1. Direct pathogen detection

To confirm a clinical suspicion of SARS-CoV-2 infection Reverse Transcription-polymerase Chain Reaction (RT-PCR) tests were developed, validated and are now the gold standard of the diagnosis of an SARS-CoV-2 infection [28]. In general the PCR enables the amplification of specific DNA-, respectively RT-PCR of RNA-, sequences. The process is only possible during exact temperatures and is divided into three steps: denaturation (94-96 degree Celsius) of the template into single strands, annealing (under 72 degrees Celsius) of the primers on each of the original strands to synthesize a new strand, extension (72 degrees Celsius) of the resulting new DNA cords from the primers [29].

Nasopharyngeal swabs are the preferred specimens for the performance of RT-PCR and viral cultures [30]. One potential problem with RT-PCR is the difficulty to distinguish between actively replicating viruses that are still infectious and non-replicating virus fragments [31]. The most reliable proof for determining actively replicating viruses, indicative of infectious activity, remains viral culture [31, 32]. Due to the laborious testing method and safety concerns, viral culture is not widely used [30]. Instead, another approach has been established in practice to characterize the infectivity of patients: The Cycle Threshold value (CT-value) describes the number of cycles needed for the proof of viral fragments in the RT-PCR. Low Ct values are indicative of a high viral load, and high Ct values are usually present in patients who are in the final stages of their infection and are unlikely to harbour viable virus [30-32].

In the course of the pandemic, rapid antigen tests as point of care testing method based on the direct detection of viral protein in respiratory samples have emerged as an area-wide testing option. Antigen testing is a useful diagnostic tool for rapid initial pre-testing and when PCR testing is not available [33]. These are commercialized by a large number of different companies, which are expected to fulfil certain specifications with regard to sensitivity and specificity [33].

2.3.2. Serological testing methods

Serological testing methods can indirectly determine contact with specific pathogens by antibody detection and have proven useful in a cross-sectional approach in

determining prevalence, underreporting, and immune response of a population in a multitude of infectious diseases encompassing SARS-CoV-2 infections. Clear statements about the correlation of antibody levels in individuals with SARS-CoV-2 with timepoint of infection and protection against re-infection remain a subject of scientific debate [34, 35]. However, studies indicate a correlation between the presence of neutralizing antibodies and a protective immune response [36, 37]. In most COVID-19 patients', seroconversion is described in week 2 after symptom onset [38, 39].

At the timepoint of the KoCo19 studies, several serological assays still differ in sensitivity and specificity. To detect a past SARS-CoV-2 infection, test formats such as ELISA (Enzyme Linked Immunosorbent Assay) and CLIA (Chemiluminescence Immunoassay) are available for detecting IgM-, IgA-, IgG- or overall antibodies.

2.4. The Prospective COVID-19 Cohort Munich (KoCo19)

In the beginning of 2020, increasing numbers of people in Germany were infected with SARS-CoV-2, thus the prospective cohort study KoCo19 (Prospektive COVID-19 Kohorte München/ Prospective COVID-19 Cohort Munich) was implemented. Its aim was to determine the prevalence of the infection within the population of Munich, to investigate the risk factors of SARS-CoV-2 seropositivity, and to elucidate the dynamics of SARS-CoV-2 infections in households in the city of Munich [40]. Personal data was collected using the OpenDataKit (ODK) tool. The first results published in March 2021 ("Prevalence and Risk Factors of Infection in the Representative COVID-19 Cohort Munich") describe the seroprevalence of the KoCo19-cohort consisting of n=5313 individuals recruited via random route methodology from n=2994 household following the first wave [41].

To investigate the immunological response in detail of individuals infected with SARS-CoV-2, a sub-study of the population-based prospective cohort was initiated in April 2020, KoCo19-Immu (Prospektive COVID-19 Kohorte München/ Prospective COVID-19 Cohort Munich – Immunology). Individuals that recently tested positive by RT-PCR and their household members were included, either from the above-mentioned KoCo19-cohort or that tested positive at the DIDTM. Study visits were conducted weekly during the first month, and subsequently monthly, to obtain a precise overview on serological, clinical and viral characteristics over time. The

manuscript “The interplay of viral loads, clinical presentation, and serological responses in SARS-CoV-2 – Results from a prospective cohort of outpatient COVID-19 cases” describes the virological loads at baseline and overtime, and associates these with clinical presentation and serological responses within the KoCo19-Immu cohort.

A number of other studies were conducted under the umbrella of KoCo19, including KoCo-19-Immu, KoCo19-Index, KoCo19-Shields, contributing to a better understanding of several aspects of the SARS-CoV-2 pandemic in the city of Munich.

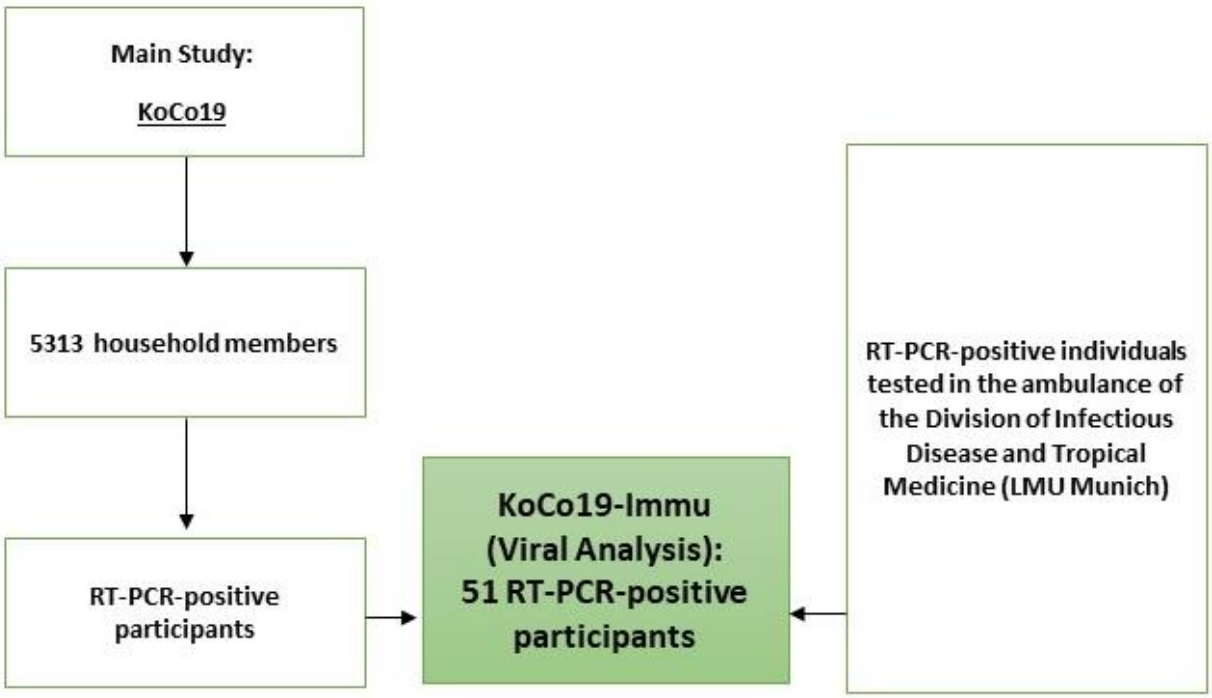

Figure 2: Participant composition for KoCo19-Immu (Viral Analysis).

3. Summary of both publications

Background

The disease COVID-19, brought on by SARS-CoV-2, was initially described in the province Wuhan, China and is still present in the world today. The first cases were detected in the end of 2019, by the beginning of the year 2020 the disease had spread worldwide, including Germany, where cases increased rapidly. Consequently, the prospective population-based cohort study (KoCo19) was implemented to examine the serological prevalence of SARS-CoV-2 in the population of Munich.

Methods

Started in April 2020, KoCo19 described the seroprevalence of SARS-CoV- during the first wave (April 2020 – June 2020). In the main-study, a total of 5313 participants of representative Munich households were recruited via random route methodology. Besides serological analysis (venous blood donation) to estimate seroprevalence, both household and personal data was collected with the OpenDataKit (ODK) tool. For further viral analysis, the prospective sub-study KoCo19-Immu was initiated and recruited between May and December 2020. 51 RT-PCR-positive individuals and their household members were included. RT-PCR and viral culture were performed using nasopharyngeal swabs, in addition to venous blood samples to test four different serological assays and clinical questionnaires at protocol defined timepoints.

Results

During the first wave the seroprevalence in Munich was 1.8%, however it increased to 3.6% during the second wave from November 2020 to January 2021 [43]. The immunological analysis in the sub-study KoCo19-Immu showed that RT-PCR-positive participants with high viral loads had a higher risk for a severe symptom progression (WHO 3: median VLs 7.45 [log10 copies per millilitre] and WHO 1 and 2: 3.78 [log10 copies per millilitre]) and exhibited a stronger immune response (in the Ro-N-Ig-test) throughout. A short STT (Symptom to test time, meaning the time between symptom onset to PCR-test) and high viral loads are positively correlated with a higher probability of a positive viral culture (median time for positive viral

culture: 5 days after symptom onset; positive samples had higher VLs: KW p = 0.0002).

Conclusion

In summary, the main study pointed out the status quo of the infection rate during the first wave in Munich in 2020, only approximately 1.8% were infected with SARS-CoV-2. The viral analysis in the prospective sub-study KoCo19-Immu showed that especially in the beginning of the infection high viral loads can be measured and then decrease over time. Furthermore, high viral loads can be associated with a strong immune response and intense course of disease. This knowledge can provide assistance for the development of quarantine measures.

4. Zusammenfassung beider Veröffentlichungen

Hintergrund

Die Infektionskrankheit COVID-19, hervorgerufen durch das Virus SARS-CoV-2, welche Ende 2019 ihren Ursprung in der Provinz Wuhan in China nahm, hat die ganze Welt bis heute im Griff. Anfang des Jahres 2020 hatte sich die Infektionskrankheit bereits weltweit ausgebreitet, auch in Deutschland nahmen die Fälle rasant zu. Daraufhin erfolgte im April 2020 der Startschuss für die Kohortenstudie KoCo19, um die serologische Prävalenz und die Dunkelziffer in der Münchner Bevölkerung zu bestimmen.

Methodik

Die KoCo19 Studie startete im April 2020, in der ersten Veröffentlichung zu KoCo19 wurde die erste Welle (April 2020 – Juni 2020) beschrieben. In dieser Zeit wurden in der Mutterstudie KoCo19 5313 Teilnehmer in München mit Hilfe einer Random Route Methode rekrutiert. Serologischen Analysen (venöse Blutentnahme) zur Bestimmung der Prävalenz wurden durch Fragebögen (OpenDataKit [ODK]) über persönliche Daten, wie zum Beispiel die Wohnsituation, ergänzt. Die Rekrutierung für die virologische Analyse in der Substudie KoCo19-Immu fand im Zeitraum von Mai-Dezember 2020 statt, in welche insgesamt 51 RT-PCR positive Probanden eingeschlossen wurden. Für die Durchführung der RT-PCR und Anzucht von Viruskulturen wurden nasopharyngeale Abstriche entnommen. Zusätzlich wurden venöse Blutproben für die Analyse in vier verschiedenen serologischen Assays gewonnen. Sowohl die virologischen als auch die serologischen Proben wurden zu definierten Zeitpunkten analysiert und durch klinische Fragebögen ergänzt.

Ergebnisse

Während der ersten Welle war die Prävalenz in München bei 1.8%, wohingegen diese von November 2020 bis Januar 2021 auf 3.6% anstieg [43]. Die immunologische Analyse in der Sub-Studie KoCo19-Immu zeigte, dass RT-PCR-positive Teilnehmer mit hohen Viruslasten ein höheres Risiko für einen schwereren Symptomverlauf hatten (WHO 3: mediane VLs 7,45 [log10 Kopien pro Milliliter] und WHO 1 und 2: 3,78 [log10 Kopien pro Milliliter]) und im Verlauf eine stärkere Immunantwort aufwiesen (im Ro-N-Ig-Test). Eine kürzere STT („Symptom to test

time“, also die Zeit zwischen Symptombeginn bis zum PCR-Test) und hohe Viruslasten sind assoziiert mit einer höheren Wahrscheinlichkeit einer positiven Viruskultur (mediane Zeit für eine positive Viruskultur: 5 Tage nach Symptombeginn; positive Proben hatten höhere VLs: KW p = 0,0002).

Schlussfolgerung

Die Hauptstudie KoCo19 gab einen fundierten Überblick über den Stand der damaligen Durchseuchungsrate in einer repräsentativen Stichprobe der Münchner Bevölkerung, ca. 1.8% waren während der ersten Welle infiziert. Die prospektive Substudie KoCo19-Immu konnte diese Erkenntnisse mit wichtigen Informationen über die Dynamik und den Verlauf von Viruslasten und Immunantworten ergänzen. Hohe Viruslasten zeigten sich vor allem am Beginn einer akuten SARS-CoV-2 Infektion und nahmen im Verlauf rasch ab. Sie waren mit stärkeren Symptomverläufen und höheren Antikörperkonzentrationen assoziiert. Dieses Wissen kann einen Betrag zur erfolgreichen Entwicklung und Verbesserung von Quarantänemaßnahmen leisten. Weiterführende Studien zum tiefergehenden Verständnis vom Ausmaß und der Dauer der Immunantwort sind nötig.

5. Publication I

Prevalence and Risk Factors of Infection in the Representative COVID-19 Cohort Munich; Int J Environ Res Public Health. 2021 March 30; 18(7):3572. doi: 10.3390/ijerph18073572

Michael Pritsch, Katja Radon, Abhishek Bakuli, Ronan Le Gleut, Laura Olbrich, Jessica Michelle Guggenbühl Noller, Elmar Saathoff, Noemi Castelletti, Mercè Garí, Peter Pütz, Yannik Schälte, Turid Frahnow, Roman Wölfel, Camilla Rothe, Michel Pletschette, Dafni Metaxa, Felix Forster, Verena Thiel, Friedrich Rieß, Maximilian Nikolaus Diefenbach, Günter Fröschl, Jan Bruger, Simon Winter, Jonathan Frese, **Kerstin Puchinger**, Isabel Brand, Inge Kroidl, Jan Hasenauer, Christiane Fuchs, Andreas Wieser, Michael Hoelscher, and on behalf of the KoCo19 study group**.**

6. Publication II

The interplay of viral loads, clinical presentation, and serological responses in SARS-CoV-2 – Results from a prospective cohort of outpatient COVID-19 cases; Virology. 2022 Apr; 569: 37–43. Published online 2022 Feb 18. doi: 10.1016/j.virol.2022.02.002

Kerstin Puchinger, Castelletti Noemi, Raquel Rubio-Acero, Christof Geldmacher, Tabea M. Eser, Flora Deák, Ivana Paunovic, Abhishek Bakuli, Elmar Saathoff, Alexander von Meyer, Alisa Markgraf, Philline Falk, Jakob Reich, Friedrich Riess, Philipp Girl, Katharina Müller, Katja Radon, Jessica Michelle Guggenbuehl Noller, Roman Wölfel, Michael Hoelscher, Inge Kroidl, Andreas Wieser, Laura Olbrich

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8. Table of figures

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