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Research Article

A Study Monitoring COVID-19 in Patients from Positive to Negative Viral Pathogen Carriage Via RT PCR and Appearance of Immunological Markers

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Abstract

The case demographics of a twenty-eight patient sample size revealed that most of the COVID-19 infected individuals in our study were aged 40 - 59. The period of time from initial PCR viral carriage to absence of viral carriage varied from six to thirty-seven days. The interval of time between a negative PCR viral carriage to the initial appearance of IgG antibodies to COVID-19 antigens varied from four to thirty five days. The absence of IgG antibodies to COVID-19 antigens was seen in only three of our sample population after 21, 33 and 61 days after the initial appearance of IgG antibodies. The presence of detectable IgG antibodies in the remaining 24 patients persisted after more than 60 days from their initial appearance. In one twenty year old patient, detectable IgG Antibodies to COVID-19 Antigens were present 90 days from their initial appearance. The presence of IgG antibodies to COVID-19 antigens could perhaps be a useful marker to determine if the virus has spread to anatomical locations beyond the respiratory tract. It is important to address the issues of viral pathogen carriage, as well as, the presence of antibodies to COVID-19 Antigens. It is important to address the issues of viral pathogen carriage, as well as, the presence of antibodies to COVID-19 Antigens.

Keywords: *COVID-19; Viral Pathogen Carriage; RT PCR; Immunological Markers*

Introduction

Coronavirus COVID-19 is a highly infectious disease that is spread from person to person by respiratory droplets generated by coughing, sneezing or aerosol transmission generated by oral communication [1,2]. COVID-19 was first identified in Wuhan, China in 2019 [3].

The viral infection is frequently associated with such symptoms as: fever, dry cough, fatigue and shortness of breath [4]. The disease symptoms often begin to appear around 2 - 14 days from the time of exposure [1-4]. The bulk of the cases associated with COVID-19 viral infections are associated with mild symptoms, however, this viral pathogen can develop into pneumonia with a progression into multi-organ failure leading to death [1-4]. The literature has reported recently reported that there also can occur neurological ramifications in COVID-19 infections [4-8].

Viral carriage of COVID-19 is detected by Real-time RT-PCR (Reverse Transcriptase Polymerase Chain Reaction) testing which currently utilizes throat and nasal swab specimen types [9-11]. In the USA and elsewhere in the world the demand for genetic based testing systems for detecting viral carriage of COVID-19 are being overwhelmed due to the continued rise in cases of COVID-19 [11].

This has led to shortages in genetic based assays and the reagents associated with these systems [11]. Thus, the application genetic testing for viral carriage in most instances has been restricted those individuals who are manifesting advanced symptoms of COVID-19 [11]. Individuals who are asymptomatic or pre-symptomatic but are highly infectious often go undetected [11].

This situation of shortages in genetic based assay reagents, and delays in the receipt of genetic based testing results by off site labs, has led to the rise of immunological testing assays which detect exposure to COVID-19 antigens. Immunological testing involves the application of ELISA Assays which are usually performed by off site labs [11].

More recently, inexpensive qualitative immunological assays have been developed and approved by the FDA for use as "point of care" testing systems which and be performed in a doctor's office [11]. Individuals who test positive for the immunological assay are indicative of having had a prior exposure to COVID-19 antigens. These individuals must then be subsequently tested in order to determine actual viral carriage of COVID-19 [11].

Roos reported that Chinese investigators have recently reported that antibodies derived from patient sources in populations consisting of convalescing asymptomatic and symptomatic patients, antibodies quickly faded [12].

This Chinese study consisted of 37 asymptomatic and 37 symptomatic patients [12]. These investigators found that in more than 90% of the patients in the asymptomatic and symptomatic patients there occurred a steep decline in IgG antibody levels of SARS-COV-2- after a period of 2 to 3 months from the initial onset of COVID-19 infection [12].

Our investigation differed from earlier investigations in that we have included both patient COVID-19 viral pathogen carriage information starting from Positive to Negative Viral Pathogen Carriage (RT PCR Assays) as well as the appearance, disappearance or continued presence of detectable levels of IgG Antibodies to COVID-19 Antigens.

Materials and Methods

This study was a cohort observational study involving a sample size of population consisting of 28 patients of both genders ranging in age from 18-71 years of age.

Patients were identified by creating number identifier codes for each patient in this study.

Dr Pathak Principal Investigator, and Ms Smith Clinical Research Assistant, were thus the only persons with the actual knowledge of the true identities of the patients in this study, and they were the only ones that had access to the number codes/true identity information.

The patients in this study manifested a variety of symptoms ranging in severity. These patients manifested such symptoms as: a) cough, b) shortness of breath, c) GI issues, d) fever, e) loss of taste, f) loss of smell and g) fatigue.

The majority of these patients had their first nasal swab viral carriage assay (RT-PCR Assay) within one to seven days from onset of symptoms, with a few outliers. The nasal swab/throat samplings were performed in a "Drive Through" setting, and the samples were then sent to off site labs (i.e. LabCorp or Quest Labs) for testing of samples.

When a negative viral carriage (RT-PCR) was achieved, a peripheral blood sample was drawn, and the patients were then tested for the initial appearance of IgG antibodies to COVID-19 antigens.

After the initial appearance of IgG antibodies to COVID-19 antigens were observed, the patients were then retested at 3 week intervals (+ 21 days) for the presence of IgG antibodies to COVID-19 antigens over a period of +60 days.

All graphical depictions were created with the aid of a Slidewrite Plus Software Program.

The statistical analyses were performed with the aid of a Statistix Software Program.

Results

Case demographics

Our patient case sample size of twenty seven individuals consisted of five age groupings (i.e. a) 18 to 29 yrs, b) 30 to 39, c) 40 to 49, d) 50 to 59, e) 60 to 71). The age groupings of 40 to 49 and 50 to 59 made up the majority of our patient cases infected with COVID-19. These two age groups each consisted of 10 patients per age grouping. The least number of cases of infected individuals were found in the 60 to 71 age group. This group consisted of only two infected individuals (See table A and figure 1).

Age Groupings	Number of cases per Age Grouping
18 to 29	3
30 to 39	3
40 to 49	10
50 to 59	10
60 to 71	2

***Table A**: Case demographics.*

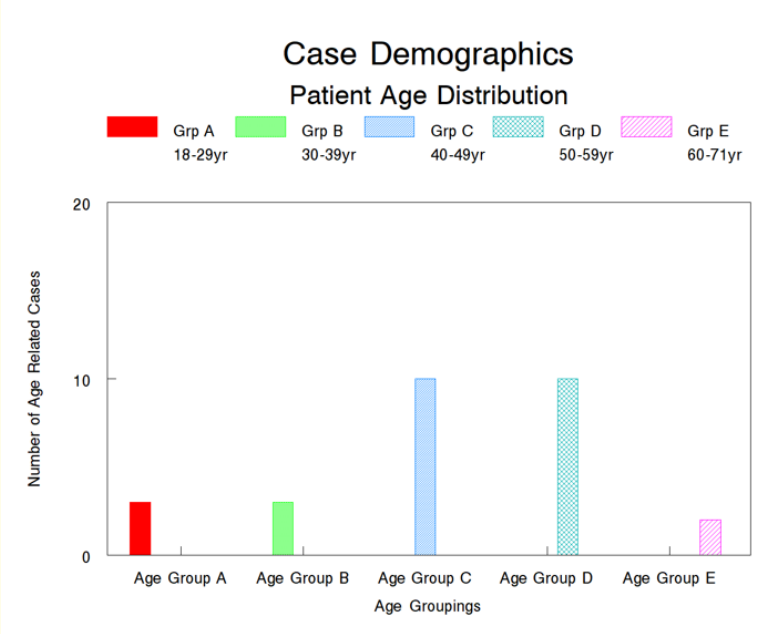

Figure 1

Time to negative COVID-19 viral carriage via PCR assay

A negative COVID-19 viral carriage via PCR from the initial positive viral carriage was observed from six to thirty seven days.

The mean value of time to negative viral carriage was 19.786 days with a standard deviation value of 6.9194 (See table B and figure 2).

Patient Identifier Code	Age of Patient	No. Days to Neg. PCR/Viral Carriage from initial Positive Viral Carriage PCR
001	45	12
002	57	21
003	54	21
004	47	21
006	42	29
007	59	26
008	23	21
009	59	22
010	56	15
011	45	24
012	50	20
013	55	13
015	49	27
016	51	13
017	34	13
018	41	29
019	48	13
021	39	21
026	44	21
027	44	06
029	60	37
031	56	21
032	58	30
034	47	17
035	18	14
036	34	19
039	71	18
040	20	10

Table B: *PCR/COVID-19 viral carriage data.*

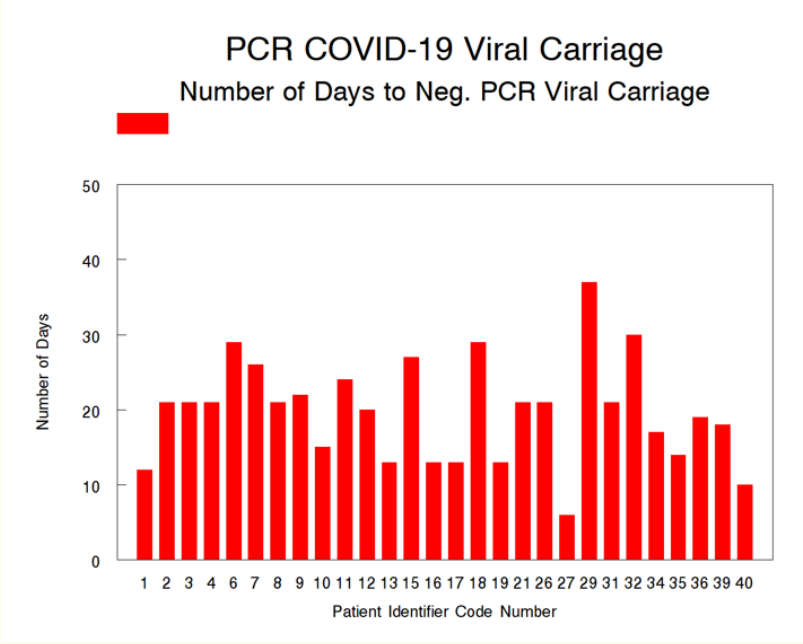

Figure 2

Time from negative COVID-19 viral carriage to appearance of initial detectable presence of IgG antibodies to COVID Ag

The presence of initial detectable IgG Antibodies was observed from 4 to 35 days after a negative COVID-19 viral carriage PCR Assay, with a mean value of 13.964 days and a standard deviation value of 8.6216 days (See table C and figure 3).

Patient Code	Patient Age	No. Days from Neg PCR to Appearance of First Detectable Presence of IgG Antibodies
001	45	15
002	57	14
003	54	04
004	47	10
006	42	08
007	59	07
008	23	07
009	59	05
010	56	08
011	45	09
012	50	12
013	55	08
015	49	15
016	51	29
017	34	30
018	41	15

019	48	15
021	39	10
026	44	07
027	44	22
029	60	07
031	56	16
032	58	06
034	47	33
035	18	35
036	34	10
039	71	19
040	20	15

Table C: *Number of days from negative PCR/COVID-19 viral carriage to the initial presence of detectable igg antibodies to COVID-19 related antigens.*

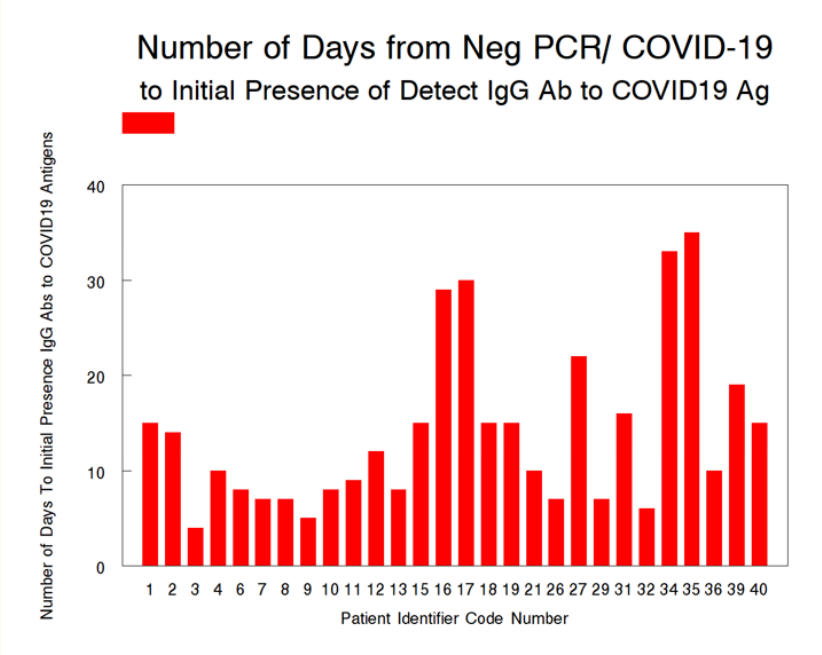

Figure 3

Duration of presence of IgG

Our investigation monitored the presence of detectable IgG Antibodies from their initial appearance, to their disappearance or their continued presence over a period of + 60 days. During this interval of time it was observed that among our patient sample population of

twenty-eight patients, there was a disappearance of detectable antibodies (21, 33, 61 days) in three patients (See table D and figure 4). In 24 patients detectable antibodies were still present after + 60 days after the initial appearance of detectable IgG antibodies. One patient was observed to have detectable IgG antibodies after a period of ninety from the initial appearance of IgG antibodies (see discussion section) (See table d and figure 4).

Patient Identifier Code	Age of Patient	No. of Days from First Appearance of Detectable of IgG Antibodies to Absence of Detectable Presence of IgG Antibodies	Continued Detectable IgG Beyond 61 Days from First Appearance of Detectable IgG Antibodies
001	45		61+
002	57		61+
003	54		61+
004	47	21	-
006	42	33	-
007	59		61+
008	23		61+
009	59	61	-
010	56		61+
011	45		61+
012	50		61+
013	55		61+
015	49		61+
016	51		61+
017	34		61+
018	41		61+
019	48		61+
021	39		61+
026	44		61+
027	44		61+
029	60		61+
031	56		61+
032	58		61+
034	47		61+
035	18		61+
036	34		61+
039	71		61+
040	20		90

Table D: *Number of days from initial appearance of detectable IgG antibodies to COVID-19 antigens up to their absence or their continued presence in patients.*

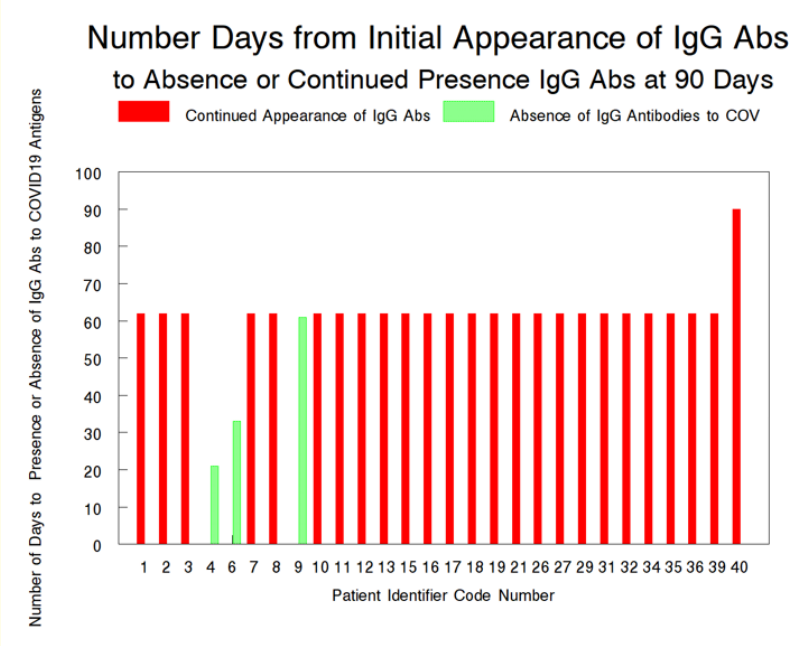

Figure 4

Discussion

Case demographics

In our patient sample population of 28 patients infected with COVID-19, the largest number of cases were observed in the age groupings of from 40 to 59, by contrast, the cases demographics cited by the Pennsylvania Department of Health has cited that their State wide surveys have reported largest number of cases involved patients from 20 to 39 [14]. This variation between our findings and those of the Pennsylvania Department of Health is that our Pike County Population consists of a larger concentration of senior citizens who are more likely to seek medical care more frequently than younger and less affluent younger residents of our county. Thus, this would account for our data being skewed in the direction of older individuals.

Time to negative COVID-19 viral carriage via PCR assay and the appearance of initial detectable presence of IgG antibodies to COVID-19 antigens

This study not only investigated length of time for a person to recover from actual viral carriage of COVID-19 as per a PCR based assay but, also look at the subsequent appearance Immunological factors in the form of the appearance of IgG antibodies following a negative viral carriage after the acute phase this infection. The investigations of Sun., *et al*. have cited the fact that "Prolonged Resistance of SAR-COV-2 RNA in Body Fluids [14]. What is interesting about the investigation of Sun., *et al*. is that they did not investigate the immunological picture in their patients because of their lack of reliable immunological test kits. The whole issue of the presence of COVID-19 antigens and their effect on subsequent patient pathology needs to be investigated [14]. The presence of specific antibodies is of importance especially as relates being potential markers for the appearance of pathological ramifications to other anatomical areas of the human body beyond the respiratory tract [4].

Duration of presence of IgG antibodies to COVID antigens

Roos has reported that investigators in China had found that the presence of in both asymptomatic and symptomatic COVID-19 patients displayed sharp decreases in IgG antibodies after a period of two to three months after the start of an infection [12].

Our investigation found that detectable levels of IgG were absent in only three patients in our sample population of twenty-eight patients (See table D and figure 4). Loss of detectable IgG Antibodies to COVID-19 antigens occurred at 21 days, 33 days and 61 days after the initial presence of IgG antibodies. Twenty three patients still displayed detectable antibodies after more than sixty days after the appearance of initial IgG Antibodies to COVID-19 antigens. One twenty year old patient still displayed detectable antibodies to COVID-19 antigens after a period of ninety days.

The disappearance or persistence of IgG Antibodies to COVID-19 Antigens after periods of sixty to ninety days perhaps could serve as a useful marker when utilized in connection with PCR based viral carriage assays as a further methodology to determine if a patient could be either cleared of viral infection, or could be liable to subsequent viral pathological manifestation in other parts of the body beyond the respiratory tract [4-8,11,15].

It is vital therefore that there is a clear understanding of the duration of detectable IgG Antibodies after an exposure to COVID-19, as well as, an understanding of the significance of these antibodies as relates to their protective properties against future re-infection with COVID-19.

Conclusion

It is important to address the issues of viral pathogen carriage, as well as, the presence of antibodies to COVID-19 Antigens. The presence of detectable IgG Antibodies could be indicative of COVID-19 infections located in other anatomical regions of the human body.

The initial findings of our investigation should be expanded to include additional patients studied over a period ninety and one hundred and twenty days after the appearance of the first detection of the IgG Antibodies to COVID-19, and the duration of detectable antibodies.

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