The Association of IgM and IgG with severity of coronavirus disease in Iraqi population

Khalid H. Abdalruda[1], Fadhil A. Nasser[2], Laith A. Younus[3], Israa K. Alyasiri[4]
[1,3,4]Department of Clinical Laboratory Sciences, Faculty of Pharmacy/ Jabir Ibn Hayyan Medical University, Al Najaf Al Ashraf, Iraq.
[2]Microbiology, Faculty of medicine / Jabir Ibn Hayyan Medical University, Al Najaf Al Ashraf, Iraq.

Abstract

Background: SARS-Cov-2 is the trigger pathogen for Coronavirus disease (COVID-19). Infected human with COVID-19 may be symptomatic with mild, moderate, severe or critical illness or asymptomatic. The serological test is valuable for affirm the infected patient who diagnosis by Real time reverse transcriptase (RT-PCR) protocol. Objective: The intended of this research is to verify the association of IgM and IgG responses against coronavirus disease 2019 (COVID-19) with severity of disease. Methods: A 159 infected patients who admitted to Hospital of AL-Sader Teaching in Al Najaf city were enrolled. The IgM and IgG levels were measured for severe and non-severe group at various time interval after symptom of onset via chemiluminescence immunoassay. Results: The data reveal significant higher level in IgG (102.5± 29.55) and IgM (15.6 ± 17.5) in sever group compared to non-severe group IgG (80.1±35.88) and IgM (9.74±14.1). Also the results exhibit that the mean ages for severe group (67.5 ± 7.5) were statistically significant older in compares with those for non-severe group (51.9 ± 15.6.6) (P value 0.001).The IgM reach maximum peak with in day 9–14 then begin decline sharply, while IgG increase over time and reach peak response from two to three week and still maintained an upward trend after 20 days then start to wane at a slower rate compare with IgM . both IgG and IgM levels show a significant elevation in severe group compared to non-severe group when tested during (15-20 days) and (21-26 days) for IgG and during (9-14days) for IgM. Conclusion: This study was concluded that IgG and IgM anti-SARSCoV-2 levels was significantly higher among severe comparison with non- severe group. In addition it was notice that the IgG and IgM were significantly increment in elderly patient.

Keywords: COVID-19, Severity of illness, IgG and IgM.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) is the prompter pathogen for Coronavirus disease 19 (COVID-19) (1)

Typical sign for COVID-19 patients embrace the elevated temperature , fatigue, sound of coughing, and dyspnea, which developed two to fourteen days after exposure.(2) About twenty percentage of infected human may develop to a severe or critical illness with more mortality rate than other cases.(3) resulting in failure in different organ and even death for patient within a short time.(4),(5) Other individuals are asymptomatic. (6)

The infected patients can exhibit antibody response to SARS-Cov-2. (7) Several studies show that the ability to detect the immunoglobulin M (IgM) and immunoglobulin G (IgG) against SARS-CoV-2 through the primary weeks after appearing the symptom of infection. (8), (9)

The first line of immune defense is represented by IgM antibody which can be detectable within three days after viral infection, after that long-term immune memory will initiate as a result of high affinity of IgG responses. (10)

The IgM antibody can be detected after onset of symptom and increase to its peak level within 2-3 week then begin to decrease while the IgG antibody continues increment and keep its level beyond seven weeks. (11)

The estimation nucleic acid of SARSCoV2 by real-time reverse transcriptase (RT-PCR) consider the established test to early identifying this infection. (12), (13) (14).But due to the false negative rate , so the miss diagnoses may occur . (7)

So, to overcome the shortcomings of viral RNA detection in individual infected with COVID-19, we decide to use anther accurate and rapid protocol depend on various detection principles such as serological test.

The serological test is valuable for supply the data for exclusion or confirmation COVID-19 infection in suspicious individual and for quick clinical diagnosis. (15) Al so use for evaluating the treatments efficacy for COVID-19 disease and vaccinating process. (16)

Several studies indicated significant association between higher IgG and IgM antibody level and severity of COVID-19, So to verify this correlation, A 159 infected individual were involved in our study and test is down for antibodies using chemiluminescence immunoassay protocol. (17) .

Method

Our study was performed in Hospital of AL-Sader Teaching in Al Najaf city in which 159 infected individual who confirmed with COVID-19 through viral nucleic acid test were participated in this project. According to the presentation during hospitalization and depend on the clinical data of patient which obtained from the medical staff, the

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symptomatic cases were subdivided into two groups. The patient with critical and severe symptom were categories under severe group while the moderate and mild case were classified in non-severe group.
The severe cases has the flowing criteria:(1) Rate of respiratory ≥30/min; (2) the percentage of oxygen saturation ≤93% during rest while the patient with critical sign: has (1) Failure of respiration and demanding mechanical machine for ventilation;(2) Shock; (3) failure some of organ that needed for ICU care.
Serum samples were collected firstly after admission (after sub classification) and secondly during period of hospitalization from day3 - day38 and tested for IgG in addition IgM against the SARS-CoV-2 utilized chemiluminescence immunoassay (17).
To explore the alteration in antibody level with disease progress level dynamically was monitored. This work was accepted by the Ethics Committees of AL-Sader Teaching hospital. The patients signed informed consent forms.

Biostatistician analysis

The data were revealed as Mean ± SD. Student's t-test, was applied to verify the differences among the severe and non-severe group in patient with COVID-19 .The significant differences was accept when the P-value less than 0.05.

Results

A 159 COVID-19 infected human were participated in this study and were classified depend on severity of disease into ninety eight (98) patient named as non- sever group which included the mild and moderate case and represent 61.64% with mean age stander deviation of(51.9 ± 15.6),and sixty one (61) patient with severe and critical illness and included under sever group and represent 38.36% with mean age stander deviation of (67.5±7.5).
The data demonstrate significant differences between for IgG level (80.1 ± 35.88) in non-severe and (102.5± 29.55) in severe group ,p-value (0.001), and for IgM level was (9.74 ± 14.1) in non-severe and (15.6 ± 17.5) in severe with p-value of (0.03) .
To investigated the dynamical change for the antibody responding ,we collected the data in different period, day 3–8 ,day 9–14, day 15–20, day, 21–26, day 27–32 and lastly day 33–38 the result show significant difference in IgG level when testing during (day15-20 and day21-26) with p-value (0.001) and failure to show significant differences in other period as noticed in (table 2),while the data of IgM shown significant differences only during day 9–14 with p-value (0.03) as in (table 3)

Table 1. Clinical result of 159 patient hasCOVID.19

Parameter	Non sever group (NO= 98) Mean ±SD	Sever group (NO= 61) Mean ±SD	P-value
IgG A.U/ml	80.1 ± 35.88	102.5± 29.55	0.001
IgM A.U/ml	9.74 ± 14.1	15.6 ± 17.5	0.03
Age (y)	51.9 ± 15.6	67.5 ± 7.5	0.001

Data presented as mean ± SD , Significant variation was considered when P-value was less than 0.05, NO is the number of patient

Table 2. IgG antibody level against SARS-CoV-2 during different period of time after onset of symptom in different severities of illness

Time interval	IgG AU/ml		IgG AU/ml		p-value
	NO	Non severe group	NO	Severe group	
Day 3–8	78	66.9±41.1	51	80.1±44.2	0.09
Day 9–14	88	74.9±52.9	59	90.2±47.1	0.07
Day 15–20	90	88.1±41.1	55	120.3±21.3	0.001
Day 21–26	92	85.6 ±39.8	56	116.8±34.6	0.001
Day 27–32	84	84.3±51.2	55	101.1±49.2	0.06
Day 33–38	92	80.7±49.6	57	94.2±41.92	0.077

Data presented as mean ± SD , Significant variation was considered when P-value less than 0.05, No is the number of positive sample of IgG during different time interval

Table 3. IgM antibody level against SARS-CoV-2 during different period of time after onset of symptom in different severities of illness

Time interval	IgM AU/ml		IgM AU/ml		p-value
	N0	Non severe group	N0	Severe group	
Day 3–8	73	8.7±23	51	16±20.8	0.07
Day 9–14	88	16.1±22.8	54	24.4± 21.2	0.03
Day 15–20	79	15.4±30.1	48	20.2±28.8	0.37
Day 21–26	83	13.9±31.8	51	16.2±14.8	0.59
Day 27–32	87	10.8±15.6	56	14.1±11.7	0.15
Day 33–38	88	4.71±11.6	54	9.3±16.8	0.08

Data are presented as mean ± SD , Significant variation was considered when P-value less than 0.05, No is the number of positive sample of IgM during different time interval.

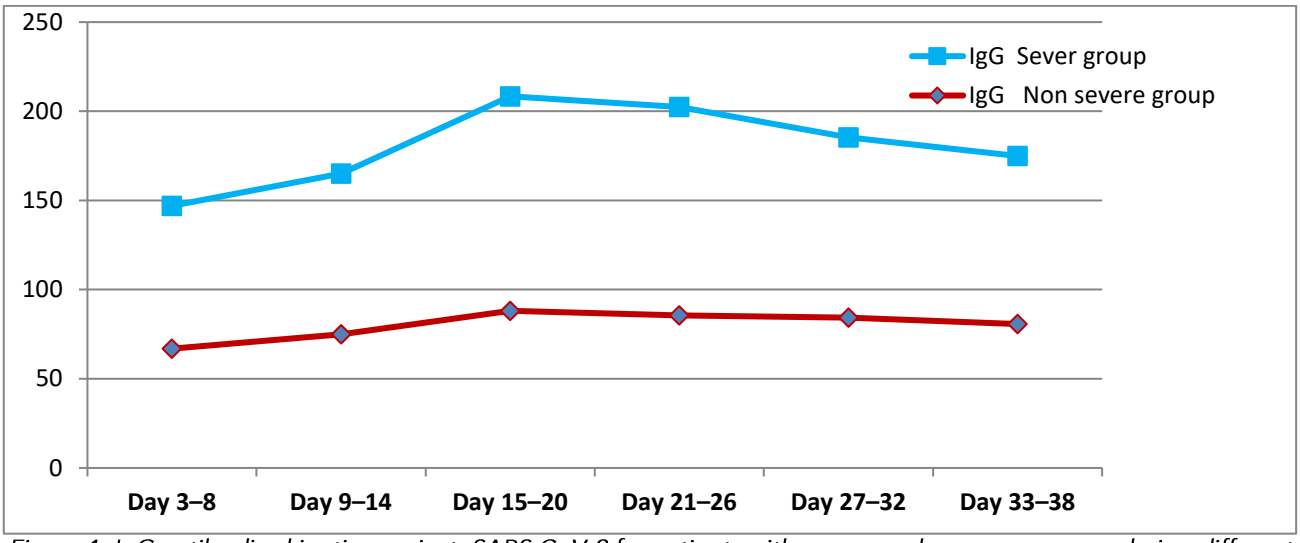

Figure 1: IgG antibodies kinetics against- SARS-CoV-2 for patients with severe and non-sever group during different time interval with COVID-19 disease

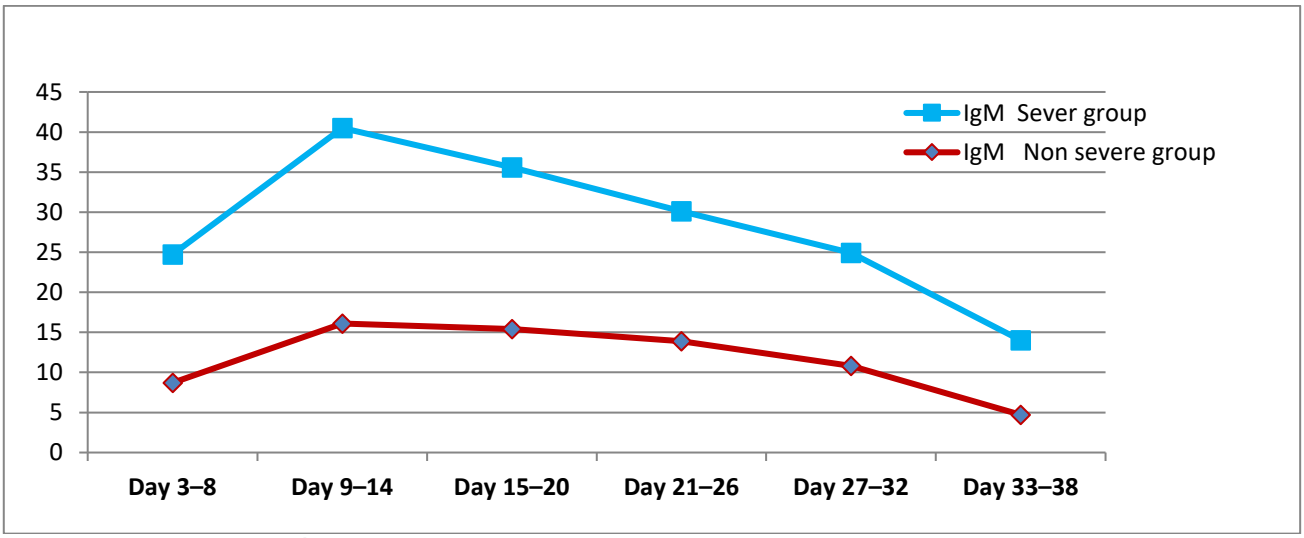

Figure 2: The kinetics of IgM antibodies against SARS-CoV-2 in patients with sever and non-sever group during different time interval with COVID-19 disease

Discussion

The serological investigation of IgG and IgM is demanding methods to confirm the doubted COVID-19 individuals with negative results for RTPCR, essential for to evaluation the degree of disease spreading (18) al so they can be utilized as an immune evidence for a former infection, an asymptomatic infection or immunization and follow up the progress of illness (19).

It is not surprising that, not all patient with SARS-CoV-2 in our study highlight positive result for IgG and IgM through different time interval which is resonate with other studies which reflected such phenomena of negative results of detectable antibody as with Liu et al. shown that 7.1% of patient does not display any significant IgG and IgM response (20). Likewise, Marklund et al. appraise forty-seven personas infected with COVID-19 and noticed that about 9.4 % not exhibit the routine IgG and IgM response (21)

So that its prefer that patient sample must be assemble another time 3-5 days later and test to examine if there is positive serological examination or elevation antibody titer. So from this point if obtain negative results for IgM plus IgG to SARS-CoV-2 , we did not exclude probability of infected with SARSCoV-2.

Different studies exhibits that antibody against the SARS-CoV-2 initiated after 3 days from onset the symptom of infection (22). So in our study we start to collect the sample after 3 days from onset of symptom under different period of time.

The data obtain from (table 1) reveal significant differences in IgG (102.5± 29.55) in sever group compared to non-severe group (80.1 ± 35.88) (P value 0.001). Al so exhibits significant differences in IgM (15.6 ± 17.5) In sever group compared to non-severe group (9.74±14.1) (P value 0.03). And these results draw a powerful positive link among the COVID-19 severity and IgG antibody titer (23).

To study the dynamics changes in IgM and IgG in different severities through different time, we focus on collecting the serum sample at various period of time. The positive sample for IgG and IgM for severe and non-sever group were mention within (table 2) and (table 3) starting from day 3 to day 38 .

In the line with prior studies, we found that there is IgM titer reaction to SARS-CoV-2 development firstly

and reach maximum peak earlier than IgG response with in day 9–14 as show in (figure 2), then begin decline sharply, while IgG increase over time and reach peak response from two to three week and unlike IgM, the IgG still maintained an upward trend after 20 days then start to wane at a slower rate compare with IgM as show in (figure 1) .

Our data is computable with observation of Andrea et al. who observed that IgM reach peak value at 10–12 days and then decrement after 18 days (24) while IgG has been reported to continues over 49 days (25).

The dynamic profile of IgG levels during time interval as in (table 2) was show a significantly elevated when tested during (15-20 days) in severe patients (IgG 120.3 ± 21.3) compared to non-severe group (88.1 ±41.1 (P value 0.001). And through (21-26 days) (IgG 116.8 ± 34.6) in severe compared to non-severe group (85. 6 ±39.8) (P value 0.001). While the other result not exhibit significant differences in IgG level through other period of time .From other hand IgM demonstrate significant higher level in severe group (24.4± 21.2) compared to non-severe group (16.1±22.8) (P value 0.03) during (9-14days) as (in table 3) .

Our findings are mirror of several evidence that indicated the titer of IgG and IgM in severe case was increment in compares with non-severe case. Qu et al and Long et al express that severe patients exhibit greater IgM and IgG responses than non-severe case (26), (27) and this because of a higher level of COVID-19 load in severe case (28). Al so Liu ZL concluded that IgM and IgG levels were lower in non-severe in compares to severe cases (29)

Our observation also indicated that the mean ages for severe group (67.5 ± 7.5) were statistically significant older in compares with those of non-severe group (51.9 ± 15.66) (P- value equal to 0.001) as shown in (Table 1).

And this reflected the correlation between the age and severity of illness in patient with COVID-19, which is agreement with other studies which concluded that ,the possibility of death in elderly infected patient due to complication in severe case is significantly higher compare with non-severe case (30),(31), especially in those with chronic disease such as hypertensions, respiratory disease and diabetes (32),(33).

There are some limitation in our study, Firstly small sample size second the patient with asymptomatic SARS-CoV-2 were not participated in this study.

Conclusion

Determination the antibody has significant role in diagnosis COVID-19.

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