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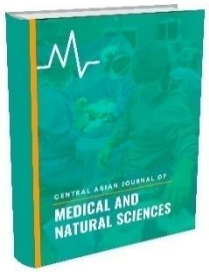

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The Association Between Vitamin D Level with IgA Plasma Level in Pregnant COVID-19 Patients

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Abstract: Background: Coronavirus disease (COVID-19) has emerged as a harmful pandemic this century, brought on by severe acute respiratory illness coronavirus-2. An ecological study has shown that greater levels of vitamin D intake are inversely linked with the occurrence and/or death of COVID-19 in communities with a genetic predisposition towards low micronutrient levels. IgA, the predominant immunoglobulin of the respiratory system, is the main entry point for a variety of bacteria..

Aim: The IgA plasma levels of COVID-19 pregnant patients were examined to see if there was a relationship with their vitamin D levels..

Patients and methods: At Bint -Alhuda teaching hospital, Obstetrics and Gynecology department and a private obstetrical clinic carried out a case control study from January to December 2022 to compare the levels of vitamin D and IgA in pregnant women with COVID-19 to those who did not have the virus. The study's objective was accomplished using a sample of 179 patients split into two groups. Group B comprised 77 healthy pregnant women who served as the control group, while Group A comprised 102 pregnant women who had COVID-19 at any point throughout their pregnancy...

Results: The mean of trimester, parity, family history of COVID-19, presence of COVID-19, and immunization history were found to differ significantly ($p<0.05$) in this study. When compared to the control group, pregnant women with a COVID-19 infection were shown to have significantly reduced levels of vitamin D and IgA ($P=0.0001$). It's interesting to note that, independent of group, a small but statistically significant positive association was found between both Vit D levels and IgA levels. Further investigation revealed a

correlation between an IgA level above >2.1 and a case's sensitivity of 72%, specificity of 63%, and accuracy of 68%..

Conclusion: COVID-19 infection among pregnant women was found to result in lower levels of Vitamin D and IgA. Both groups showed significant correlation between levels of Vit D and IgA..

Key words: Covid -19, Immunoglobulin A (IgA), vitamin D level, and pregnant women.

Introduction

1. The Coronavirus Disease 2019 (COVID-19)

The story began in Wuhan City, Hubei Province, China — an unexpected outbreak of respiratory illness hit the 9.4 million city hard. Gradually leading us to discover a new foe lurking in our midst – COVID-19 or as technically termed severe acute respiratory syndrome coronavirus 2 (earlier known as 2019-nCoV) [1]. It was New Year's Eve, December 31st when WHO got wind of this silent killer spreading its reach across borders. After scarcely less than a month and hundreds more affected by it, WHO sounded the alarm bell with an official declaration—the happening was no longer just an outbreak but a global health emergency on January 30th.Then came March – and pandemic it was! On March 11th - COVID-19 had swept over countries marking itself quite violently throughout humanity's historical timeline since such significant classification has not been necessitated post H1N1 influenza in '09[2]. The name 'COVID-19', was selected so as to dodge any perceivable stigmatization of a given locale, an ethnic group, or even association with animals [3]. On February 11th of the year 2020, a new virus - christened SARS-CoV-2 - burst onto the scene by courtesy of The International Committee on Taxonomy of Viruses' Coronavirus Study Group's official report [4]. Albeit experts within the medical fraternity still grapple with inadequate knowledge concerning COVID-19's potential implication on neonates from infected mothers. Evidence does hint at pregnancy potentially accelerating progression rate for this viral infection [5,6]. A handful number studies reveal that severity could span anywhere between mild symptoms and in extreme cases resulting in fatality. While around 16% of cases seem to manifest a severe illness, quite a few experts argue that majority of COVID-19 infections aren't so critical. Folks who are more likely to face a serious bout of COVID include the oldies, those with weakened immunity and individuals dealing with certain health conditions such as diabetes, heart issues or breathing troubles[7]. Now we're talking about folks back in July 2020 when WHO dropped the bombshell - stating there's possibility airborne transmission plays key role in this virus spreading like wildfire! And just like that suddenly there was huge emphasis on wearing masks and maintaining social distancing for prevention [8]. In addition, we've noted the virus's ability to persist and maintain its infectivity on surfaces for differing time spans. Citing a particular investigation, SARS-CoV-2 may still be identifiable up to 72 hours later upon certain surfaces—even when its infectious attribute has begun dwindling down some. Importantly though, after just four short hours, copper boasted zero trace of live SARS-CoV-2. On cardboard too; empty it was after no more than 24 hours [9].

2. The role of IgA in COVID-19

Two distinct subtypes of IgA exist, they're labeled as IgA1 and the other known by the designation IgA2. Let's start with where you'll likely encounter monomeric IgA1 – it is thriving in abundance within our bloodstreams. When we shift focus to the mucosal surface though, that's where dimers and

polymers of both subtypes -IgA1 and its kin- cling together by dint of J chains. Their job? Immensely vital! They form our first line defense against noxious toxins, malicious viruses - big or small - along with bacteria, neutralizing them before they attach onto the epithelium layering our mucus membranes. Notably, different spaces favor different types; airways seem partial to producing more from subtype one while colon prefers churning out copious amounts of type two. Shouldering responsibility for this mass production are none other than plasma cells nestled beneath cladding if cellular tissue—submucosa being their prime locality! From there on begins a complex journey via polymeric immunoglobulin receptors designed specifically for transporting nascently produced antibodies like these from underbelly up towards epithelial cell surfaces[10]. When it comes down to containment as well as defense against SARS-CoV-2, a lot hinges on secretory IgA. Why? Because the virus has its crosshairs fixed firmly on our body's mucosal areas. In what might puzzle some, serum IgA levels took a nosedive just four weeks after initial symptoms started showing themselves. Meanwhile, the saliva still had detectable neutralizing IgA for quite some time longer [11]. Here is another unanticipated thing by many; mothers who got infected with SARS-CoV-2 ended up creating pretty specific Secretory IgAs in their milk (sIgA's); suggestive of post-infection protective responses that - surprise again - made their way to the neonates offering protection [12]. Permit me to draw attention to IgA's multifarious roles. It interacts with mucosal epithelial cells, latches onto antigens and cellular receptors, and is a safeguard for the upper as well as lower respiratory tract mucus linings. Indisputably paramount in achieving this feat is the expansiveness of its antigen-binding range. Now, IgA shows up wearing different hats - it could be polymeric or dimeric or simplistic monomeric – each serving unique purposes. And let's not minimize this; understanding the sway that antibody avidity along with affinity hold over protective processes becomes downright crucial (13).Tocombat harmful microorganisms and dampen immune activation, B lymphocytes cast a wide net of various IgAs. The principle involved here is known as 'IgA class switching', where B cells gain the capability to express IgA. They do this using both T-dependent and independent mechanisms. However, the T-dependent method takes its sweet time—about an entire week—which can be frustratingly slow for battling those pesky mucosal infections. It's primarily the natural antibodies of the IgM isotype that neutralize infections. Y'know, their broad range and adaptable affinity kinda make these essential silent warriors. And get this! They're pumped out even before an antigen knocks on our body– playing a vital role in holding back the infection during those critical two weeks needed for high-affinity antibodies to show up[14].

3. Vitamin D and COVID-19

Consider the moment when bare skin encounters intense sunlight. What happens? It kick-starts this incredible process, manufacture of pre-pro-hormone Vitamin D3 as a result of 7-dehydrocholesterol being bathed in solar UVB rays. Sure, you know that Vitamin D plays its part in managing calcium and bones but wait - there's more! This clever vitamin has way broader influence than that alone. Also holds an important role in maintaining well-balanced immunity because it works with different immune cells such as T, B or even antigen-presenting cells who are endowed with special Vitamin D receptors allowing them to turn around and produce the active form themselves! But get this...Vitamin D can act independently too within its local immunological neck-of-the-woods [15]. Imagine taking Vitamin D supplements and feeling relieved as they lessen your risk of viral respiratory infections. We're talking about ailments like influenza, even COVID-19![16]. Vitamin D steps up to the plate by decreasing how fast viruses multiply. It encourages the production of antimicrobial peptides in our respiratory cells' lining and that mitigates just how severe a virus infection can be. But hey, it isn't all! Perhaps most noteworthy is that clever old Vitamin D fights relentlessly against the inflammatory response unleashed by SARS CoV-2 – you know, what triggers COVID? The vitamin cranks up anti-inflammatory cytokine concentrations while slowing down pro-inflammatory ones which could worsen lung damage [17]. A variety of recent studies have uncovered a link between lower vitamin D

levels and heightened risks for COVID-19. It's not just vague—we've got loads of data showing that the severity, duration, and death rate tied to COVID are all strangely connected to low vitamin D [18,19]. Damage to Organs from ARDS and in patients with the big C is actually down to the cytokine storm kicking off a tad too much oxidative stress [20,21]. You should know this intriguing bit - active hydroxyl versions of your good old Vitamin D can spark anti-oxidative responses; they trigger innate immunity against infectious foes while also easing inflammation. When the winter season rolls around, viral outbreaks tend to spike - it's down to lesser vitamin D levels. So pops up a bunch of studies claiming how taking vitamin D supplements could lower your odds of catching severe viral diseases and even take some sting out of their severity [22,23]. Now here's where it gets spicy – there's this ongoing tussle about whether 25-OH D vitamin levels have anything to do with serious COVID-19 cases cropping up. There are those who suggest that pushing Vitamin D might not help when you're with heavy-duty cases [24,25].

Patients and methods:

In ThiQar Governorate, a case-control study carried in a period from January to December 2022. The study involved measuring the plasma levels of IgA and Vit D in pregnant women with COVID-19 (N=102) and comparing them to a group of pregnant women without the infection(N=77).

Inclusion criteria:

The study population involved women who met the following criteria:

1. Adult women above 18 years old.
2. At any term of pregnancy
3. Get COVID-19 infection confirmed by PCR test.
4. Informed signed consent

Exclusion criteria:

1. Refuse to participate in this study.
2. History of previous COVDI-19 infection.

Data collected by direct interview with all respondents, the interview is done by a questionnaire which comprises; baseline demographic data at time of examination, and draws 2 ml of fresh blood from each participant .

Statistical Analysis

Version 1: Utilizing SPSS software version 23, data was input and analyzed. In order to examine the correlation between IgA and Vit D levels, a person correlation coefficient and independent sample t test were employed. The threshold for statistical significance was established as P value <0.05.

Version 2: Through the implementation of SPSS software version 23, data was entered and assessed. By utilizing a person correlation coefficient and independent sample t test, a link between IgA and Vit D levels was tested. An acceptable level of statistical significance was considered to be P value <0.05..

Results:

Table -1: Demographic characteristics of the study population

Case (N=102)			Control (N=77)		P value
Count		N %	Count	N %	
Age	Mean ± SD Range	31 ± 6.6 18 – 43 years	34 ± 6.2 19 – 42 years		0.09
Trimester	Mean ± SD Range	5.8 ± 2.1 2 – 9 months	7 ± 2.1 2-9		0.001

Trimester	1st	19	18.6%	6	7.8%	0.002
	2nd	40	39.2%	18	23.4%	
	3rd	43	42.2%	53	68.8%	
Gravida	1-2	22	21.6%	11	14.3%	0.09
	3-4	58	56.9%	33	42.9%	
	≥ 5	22	21.6%	33	42.9%	
Parity	0-2	62	60.8%	29	37.7%	0.003
	3-4	34	33.3%	34	44.2%	
	≥ 5	6	5.9%	14	18.2%	
Family history of COVID infection and Contact	No	53	52.0%	11	14.3%	0.0001
	Yes	49	48.0%	66	85.7%	
HX of Vaccination	No	77	75.5%	42	54.5%	0.003
	Yes	25	24.5%	35	45.5%	
HX of Travel	No	76	74.5%	58	75.3%	0.09
	Yes	26	25.5%	19	24.7%	

Table -2: Vit-D levels for studied groups

	cases	N	Mean	SD	P-value*
Vit-D	Case	102	13.338	6.36	**0.0001**
	Control	77	21.89	15.45	

***Independent sample t test**

Table-3: IgA level for studied group

		N	Mean	SD	P-Value*
IgA	Case	102	1.115	0.8	**0.0001**
	Control	77	2.64	1.3	

***Independent sample t test**

Table-4: Correlation of IgA and Vit D levels

		VIT-D	IGA
IGA	r	0.208	1
P value		**0.005**	
N	179	179	179

Discussion:

According to a study carried out recently, pregnant women afflicted by the COVID-19 virus were found to have markedly diminished levels of both Vitamin D and zinc [26,27]. Earlier studies had hinted that insufficient Vitamin D could indeed heighten one's susceptibility to COVID-19 infection; this was seen in non-pregnant subjects as well [28]. Therefore, maintaining adequate amounts of Vitamin D becomes critical—as it plays an invaluable role in bolstering our ability to fight off infections and honing immune responses [29]. Further, a study carried out by Ille and colleagues brought to light that nations like Italy, Spain, plus the United Kingdom—all of which suffered harsh

COVID-19 trajectories—had average serum Vitamin D levels that were notably low [30]. When contrasted with the control contingent, expectant mothers living with COVID-19 had significantly diminished IgA levels. As such evidence shows, IgA is a key player in early viral neutralization and it acts as a protective barrier against viruses infiltrating mucosal surfaces [31]. Based on research undertaken by Çölkesen et al., catastrophic manifestations of COVID-19 infection were recounted among patients suffering from severe deficiencies in their IgA counts [32].

Conclusions:

1. Vitamin D had a considerable correlation with IgA levels.
2. A meaningful association was observed between IgA levels and vitamin D.
3. IgA levels and vitamin D showed a significant link.
4. The level of IgA had a noteworthy correlation with vitamin D.
5. Among pregnant women with COVID-19, IgA levels were observed to be significantly reduced.

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Conflict of interest: No conflict of interest**.**

Consent to Participate: All participants provided written informed consent before participating in the study.

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