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Effect of COVID-19 on Severity of Signs and Symptoms of Autoimmune Diseases

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ABSTRACT

It is an observational cross-sectional study, the data collected by convenience sampling method from 33 patients in the Ranya General Hospital and private clinics for follow-up patient's autoimmune diseases state in the Ranya city from the 10th November 2020 to the 20th May 2021 and the study included all the patients had autoimmune diseases that recovered from the COVID-19 disease. For the study materials, the data was collected by a questionnaire form that included demographic and autoimmune disease questions also questions about the patient's intensity of their autoimmune disease's signs and symptoms before and after they recovered from COVID-19. Determine patient's autoimmune disease signs and symptoms intensity based on the prescribed drug for a treat the autoimmune diseases which are changed by special doctors. Furthermore, the data were analysed by SPSS software to produce descriptive statistic measures and to find the difference between dependent categorical variables Sign test were used but Chi-square test used for the categorical independent variables with regarding 0.05 as a significant critical value. The result reveals that range of their age started from 42 to 74 years old with mean± standard deviation (57.3 ± 8.06) and most of cases 15(45.5%) were between (55-65) years old, followed by less than 55 years old 13(39.4%) and more than 65 years old age 5(3.8%) cases respectively. Rheumatoid arthritis was a major type 16 (48.5%) of the autoimmune disease compared to other types, Ankylosing Spondylitis 8(24.2%) cases, and Ulcerative Colitis 6(18.2%) cases respectively while Crohn's disease was the minimum 3(9.1%) cases and before they got COVID-19 most of the cases 25(75.8%) had moderate intensity signs and symptoms of their autoimmune diseases and 8(24.2%) cases had severe signs and symptoms but after they recovered from the COVID-19 disease the rate of their signs and symptoms changed to mild 19(57.6%) and moderate 14(42.4%) intensity while severe intensity signs and symptoms were zero with highly significant differences (P-value 0.0001). Despite the current study

concluded autoimmune disease patients recovered from the COVID-19 their autoimmune diseases signs and symptoms intensity decreased significantly but still further studies needed with bigger sample size to determine and explain this association.

1. INTRODUCTION

Since 2019, a novel Coronavirus disease 2019 (COVID-19) arise in Wuhan city in the Hubei province in China, spread to clearing over the globe to be a pandemic that infects most of the countries. COVID-19 was formally announced globally widespread (pandemic) by the world health organization on March 2020. An enormously COVID-19 is a highly contagious respiratory disease which caused by SARS-CoV-2 virus. COVID-19 is a respiratory disease with extremely spreading capability caused by a virus called the SARS-CoV-2. The SARS-CoV-2 virus can spread in both direct and indirect routes, in the direct route by the droplets from the infected person when coughs, sneezes, or breaths to the non-infected person directly while the indirect route occur when the non-infected person touches a surface or an objective that is contaminated by the virus then transfer to the body ports such as mouth, nose, or eyes by infected hands. The COVID-19 most observed abnormal clinical manifestations include fever, difficulty in breathing and cough. In addition, fewer observed abnormalities are headache, fatigue, chills, body ache, sore throat, lack of flavor, runny nose, nausea or vomiting, diarrhea. The clinical manifestation's intensity may be ranked from mild to severe and the appearance of signs and symptoms need 2 to 14 days after exposure to the SARS-CoV-2 virus. The infected person with the SARS-CoV-2 virus may be asymptomatic cases but still, they have the ability to infect healthy persons when they contact directly or indirectly. [1] The majority of the infected people with COVID-19 with good health care recover without needing unique treatment, but elder people and people with chronic diseases (cancer, diabetes and a weak immune system) or serious medical disorders are at high risk of serious consequences of the disease. [2]

Autoimmunity the presence of an antibody active against a tissue constituent of the individual producing it (antibodies against autoantigens) or producing by an organism and acting against its own cells or tissues (self-reactive). lymphocytes without the induction of any pathological changes (structural and/or functional) in tissues and/or organs as a consequence of autoreactive cells. Virus infections as an environmental factor have contributed to the development of autoimmune diseases such as inflammatory arthritis, systemic juvenile idiopathic arthritis, multiple sclerosis, Sjogren's syndrome, systemic lupus erythematosus, polymyositis, primary biliary cholangitis, uveitis, Henoch Schonlein Purpura, Hashimoto thyroiditis, systemic sclerosis and autoimmune hepatitis. [3] also, there well-known viruses that cause autoimmune reaction among infected patients such as; Epstein-Barr virus (EBV), Hepatitis A and C virus, Parvovirus B19, Herpes virus-6, HTLV-1, Cytomegalovirus (CMV), and Rubella, those are specific types of viruses associated with that trigger and beginning of autoimmune conditions. [4]

The term "autoimmune disorder" describes a range of painful symptoms put on by a malfunction in the body's interconnected pattern. In autoimmune diseases, this inflammation persists, causing pains and long-term changes or damage to the tissues involved. Autoimmune illnesses are difficult to identify because they have no known cause for that frequent remission and recurrence patterns occur. [5]

Autoimmune disease is influenced by a wide range of factors (genetic and environmental factors), and the preponderance of autoimmune conditions are chronic in nature, requiring long - term treatment. Both molecular mimicry or cell mimicry have indeed been suggested as pathways for generating autoimmunity. [6]

Bystander activation is the activation of antigen-presenting cells by the infection such as virus have a role by further activating pre-primed lead to auto-reactive T-cells, final result cause tissue damage by the production of pro-inflammatory mediators. [7]

The reaction between environmental and hereditary factors influence the appearance of the autoimmune illness. the contribution of the heredity risk in the autoimmune disease is near one-third of all cases while environmental factors (non-hereditary) occupy the remaining 70% of cases of autoimmune diseases. The role of the hereditary factors is assumed to be polygenic (caused by many genes) for the majority of autoimmune disorders. On the other hand, environmental factors also have a significant role in modifying, developing and promoting autoimmune disorders. The environmental factors may trigger the beginning of the illness and they have a role in determining the nature of the first manifestations of autoimmune disease. [3]

For the direct viral damage for autoimmune diseases, only a few mechanisms such as; the production of cryptic self-peptides, bystander activation, molecular mimicry, antigenic spread and the adjuvant effect are suggested for how infections can lead to autoimmune disease. When a microorganism's antigens closely resemble self-antigens, autoimmunity is produced, according to the concept of molecular mimicry. While the immune response has been stimulated inside a non-specific way, bystander activation can also happen. [7]

There are two general types of autoimmune diseases which are organ specifics such as thyroiditis, skin diseases, reproductive diseases, hemolytic anemia, Myasthenia gravis, ophthalmic diseases, insulin dependent diabetics and neurological disease while non-organ specifics are Rheumatoid Arthritis and Polyarthritis also Systemic Lupus Erythematosus and Dermatomyositis.

Treating autoimmune diseases depend on the proper diagnosis which establish by careful clinical evaluation. General principles for autoimmune therapy are treating reversible causes of weakness, fatigue and weight loss for that first choose treatments for those patients are Non-steroidal anti-inflammatory drugs (NSAIDs) after that there are other treatment classes such as anti-inflammatory drugs (antimalarial medications (hydroxychloroquine) and Sulfasalazine) immunosuppressant drugs (Methotrexate, Cyclophosphamide and B cell suppressive therapies) and biological and molecular therapies. [8]

The main goal of the study was to determine the consequence of the COVID-19 disease on the intensity of the signs and symptoms of the autoimmune diseases among autoimmune immune patients who recovered from the COVID-19 disease.

2. METHODS AND MATERIALS

The current study is an observational cross-sectional study where the data was collected in the Ranya General Hospital and private clinics for follow-up patient's autoimmune diseases status in the Ranya city from the 10th November 2020 to the 20th May 2021. Convenience sampling method used for selecting 33 patients and the data collected by direct interview with patients and also follow-up data collected from patients file with considering patient privacy. Furthermore, the samples inclusion criteria of the study included two conditionals, first all the patients in the data collecting settings who had autoimmune diseases and second condition included those patients who recovered from the COVID-19 disease recently. For the study materials, the data collected by a questionnaire form that consists of three sections as follow; section one included questions about patient's demographic character and questions about patient's autoimmune disease type and section two contained the questions about autoimmune disease's treatment before and after COVID-19 while the last section specified for the questions about COVID-19.

Determine patient's autoimmune disease signs and symptoms intensity (level) category based on the prescribed drugs for treat autoimmune diseases which are prescribed and changed by their special physicians after full medical assessment for their autoimmune disease signs and symptoms progress in each visit (follow-up). The treatment was classified into three categories as follows; first, those who used analgesic drugs were considered as a mild level and those

who use immunosuppressant drugs (Disease-Modifying Antirheumatic Drugs (DMARDs) and Prednisone drugs) considered as a moderate level while those who used biological drugs were classified as a severe intensity level. In addition, SPSS (Statistical Package for the Social Sciences) software used for data entering and analyzing the collected data to produce descriptive statistic measures such as standard deviation, mean, percentage and frequency and to find the difference among two categorical dependent variables the Sign test used while Chi-square test were used for two independent categorical variables but if number less than 5 included in the expected value, fisher's exact test used instate of the Chi-square test with considering equal or less than 0.05 as a significant critical value.

3. RESULTS

This study included 33 persons who had autoimmune diseases and recovered completely of COVID-19 diseases in the Ranya city. The minimum age of the participates were 42 years old while the maximum age were 74 years, with the mean ± SD (57.3 ± 8.06) and most of them 15 (45.5%) were between (55-65) years old, followed by age group less than 55 years old which consist of 13 (39.4%) of the cases and more than 65 years old age group 5 (3.8%) cases respectively. Furthermore, about participates gender for the current study, 21 (63.7%) of them were male and the remaining 11 (33.3%) were female. Table 1

Rheumatoid arthritis was a major type 16 (48.5%) of the autoimmune disease comparing to other autoimmune disease types then followed by Ankylosing Spondylitis 8 (24.2%) cases and Ulcerative Colitis 6 (18.2%) cases respectively while Crohn's disease was the minimum 3 (9.1%) cases. Table 1

For the characters of the COVID-19 diseases, the mean and standard deviation of the duration of COVID-19 diagnosis were (4.7 ± 1.26) days while minimum days were 2 days duration and 6 days were maximum duration for the diagnosis and most of the cases had a moderate 30 (90.9%) COVID-19 disease's signs and symptoms and the remaining cases 3 (9.1%) had a severe signs and symptoms. In addition, only 4 (12.1%) cases out of the 33 cases with autoimmune diseases during COVID-19 diseases needed supplemental oxygen (O2). Table 1

Table 1: Demographic and diseases characters of the study participates

Variables	Groups	Frequency	Percentage
Age groups	**Lower than 55**	13	39.4
	55-65	15	45.5
	More than 65	5	15.1
Gender	**Male**	21	63.7
	Female	11	33.3
	Missing	1	3
Type of Autoimmune disease	**Rheumatoid**	16	48.5
	Ulcerative	6	18.2
	Crohn's disease	3	9.1
	Ankylosing	8	24.2
Duration of COVID-19 diagnosis (day)	**Mean ± Std.**	4.7 ± 1.26	
	Minimum	2	
	Maximum	6	
Intensity of COVID-19 signs and symptoms	**Mild**	0	0
	Moderate	30	90.9
	Severe	3	9.1

Did you need supplemental oxygen (O2) during COVID-19 disease period?	**Yes**	4	12.1
	No	29	87.9

To reveal the consequence of the COVID-19 disease on the autoimmune disease cases the patient's intensity signs and symptoms of their autoimmune were compared with intensity of the same signs and symptoms after they recovered from COVID-19 disease (comparison of autoimmune signs and symptoms before Covid-19 and after they recovered form COVID-19) between the results were as follow; before the COVID-19 most of the cases 25 (75.8%) had moderate intensity signs and symptoms of their autoimmune diseases and 8 (24.2%) of the cases had severe signs and symptoms but after they recovered from the COVID-19 disease most of them 19 (57.6%) had mild intensity followed by moderate 14 (42.4%) signs and symptoms while severe signs and symptoms were zero. In addition, the P-value difference between intensity of the signs and symptoms before and after they recovered from COVID-19 diseases among autoimmune disease cases was 0.0001 which mean highly significant difference caused (affected) by the COVID-19 disease on the intensity of the autoimmune disease's signs and symptoms. Figure 1 & 2

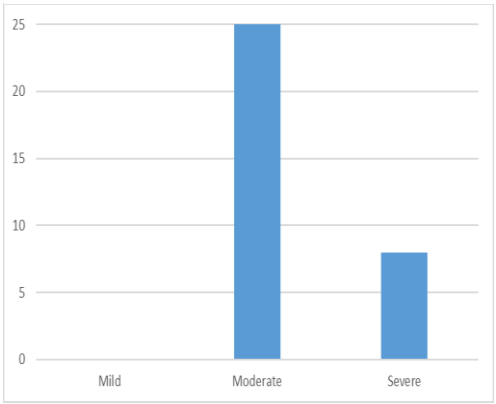

Figure 1: signs and symptoms frequency of the autoimmune diseases before COVID-19

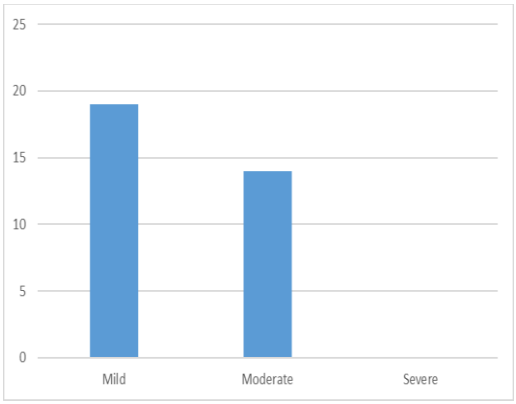

Figure 2: signs and symptoms frequency of the autoimmune diseases after COVID-19

For the correlation between variable groups with the intensity level after COVID-19, the results shows that lower age cases (42-65 years old) their intensity of the autoimmune Signs and symptoms more in the mild degree comparing to the older cases but the relationship were non-significant (P-value 0.648) and also almost in the all autoimmune diseases types the signs and symptoms of their autoimmune were at the lowest level (Mild) comparing to the more intense level (moderate) but this difference were non-significant (P-value 953). Furthermore, despite the non-significant difference between the covid-19 Intensity signs and symptoms with the autoimmune disease's signs and symptoms (P-value 0.244) but still the results show that all (3) cases who had severe covid-19 intensity signs and symptoms had lowest level (mild) of the autoimmune disease's signs and symptoms also nearly same effect observed among moderate level of the COVID-19 signs and symptoms. Table 2

Table 2: Relationships between age and COVID-19 characters groups with signs and symptoms of autoimmune after COVID-19

Variables	Groups	Autoimmune signs and symptoms after COVID-19			P-Value
		Frequency	Percentage	Total	
Age groups	Lower than	7 (53.8%)	6 (46.2%)	13	0.648
	55-65	10 (66.7%)	5 (33.3%)	15	
	More than 65	2 (40%)	3 (60%)	5	
	Total	19 (57.6%)	14 (42.4%)	33	
Type of Autoimmune disease	Rheumatoid	9 (56.3%)	7 (43.8%)	16	0.953
	Ulcerative	4 (66.7%)	2 (33.3%)	6	
	Crohn's	2 (66.7%)	1 (33.3%)	3	
	Ankylosing	4 (50%)	4 (50%)	8	
	Total	19 (57.6%)	14 (42.4%)	33	
Intensity of COVID-19 signs and symptoms	Mild	16 (53.3%)	14 (46.7%)	30	0.244
	Moderate	3 (100%)	0 (0%)	3	
	Severe	19 (57.6%)	14 (42.4%)	33	

4. DISCUSSION

The autoimmune diseases relationship with COVID-19 disease is a complex relation, there are many different conclusions been reported globally. Some studies showed that the autoimmune disease have positive effect on the COVID-19 patients such as Liu [9] study and Wang [10] study used some medications for treatment of the autoimmune diseases have therapeutic effect on the COVID-19 such as Chloroquine and Hydroxychloroquine and also other studies reported that autoimmune diseases patients those who use immunosuppressed medications compared with others not at increased risk of COVID-19 and not need special attention during disease's period to recover form COVID-19 disease. [11, 12] Moreover, COVID-19 is viral infection there are evidence showed that the COVID-19 molecular mimicry the autoimmune diseases body immune system responses.[13] On the other side, there many reports show that the autoimmune patients have higher mortality rate (death rate) especially those patients that are on the immunosuppressed medications [14] and also some studies reported that as other virus infection COVID-19 have capability to trigger autoimmune responses and develop autoimmune disease after infection which cause severe interstitial pneumonia.[15-17]

The outcome of this study reveals that most of the cases 30 (90.9%) cases had moderate degree signs and symptoms during effect by COVID-19 pandemic diseases, through the time just 3 cases (9.1%) had severe syndrome COVID-19 pandemic diseases, at the same time all the 33 cases not have mild manifestation COVID-19 universal diseases. Furthermore, only 4 (12.1%) cases out of the 33 cases with autoimmune diseases during COVID-19 diseases needed supplemental oxygen (O_2). All three cases who had severe syndrome all of them needed supplemental oxygen (O_2) and before a month they effected by COVID-19 they took biological medications. Other studies showed controversial risk of infection among autoimmune diseases cases with COVID-19 prognosis. [9]

The current study results show that before the COVID-19 most of the cases had moderate intensity signs and symptoms of their autoimmune diseases but after they recovered most of them had mild intensity followed by moderate signs and symptoms while severe signs and symptoms were zero. The decrease of the autoimmune disease's signs and symptoms among the patients who recovered from COVID-19 disease might be related to more than one factor, among those factors is that the studies on the patients who had autoimmune diseases

concluded that the some medications used for treatment of the autoimmune diseases have therapeutic effect on the COVID-19 such as Chloroquine and Hydroxychloroquine [10] and also the pathological study [18] showed that T lymphocytes (CD8+) suppressors observed in numerous numbers in the different organs among dead patients by COVID-19 by using bright lineage of immunohistochemistry, targeting CD8+ suppressers previously been used to treat autoimmune diseases. [19]

The small sample size (33 cases) and the short period data collection (type of the data collection method) also might affected the conclusion of the current study and can be considerate as the study limitations for that we recommend the studies with larger sample size longer durations (Cohort studies) to determine the relationship of the COVID-19 disease with the autoimmune disease's signs and symptoms intensity.

5. CONCLUSION

Despite the current study concluded that autoimmune disease patients who recovered from the COVID-19 their autoimmune diseases signs and symptoms intensity decreased significantly but still further studies needed with a bigger sample size to determine and explain this association. Also, the current study concluded that in the lower age groups (42-55 years old) intensity of the autoimmune disease's signs and symptoms decreased more compared to the oldest patients after they recovered from COVID-19 and among the majority of the autoimmune disease types, the intensity of the autoimmune disease's signs and symptoms decreased to the lowest (mild) level after COVID-19.

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