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Assessing Respiratory Muscles strength as a Biomarker of Lung Function among Patients with Rheumatoid Arthritis, King Saud Medical City

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ABSTRACT

Background: Assessment and evaluation of the strength of the respiratory muscles are beneficial in some clinical conditions, Rheumatoid arthritis is an articular disorder with extra-articular manifestations affecting other organs and tissues and worsening prognosis. Pulmonary system involved in about 30-40% of RA patients. The objective of this study is to assess respiratory muscles strength as a biomarker of lung function among asymptomatic patients with rheumatoid arthritis. *Patients and Methods:* It was analytical, facility-based study at pulmonary function test lab, department of respiratory care at King Saud Medical City (KSMC). Patients confirmed with rheumatoid arthritis, according to ACR /EULAR were selected with age group 18-75 years-old. Pulmonary function tests were carried out using MasterScreen PFT spirometer (CareFusion, Hoechberg Germany manufacture). The machine was calibrated daily .We used of the MicroGard ® mouthpieces containing filter to prevent the infections. *Result:* A total of 70 participants in the age range 18-75 years enrolled in the study. Out of 70 participants, 14.3% of the study participants were male subjects while 85.7%were female subjects. Saudis constituted 88.6% of the participants were Saudis and 12.4% non-Saudis. The distribution of the chronicity of rheumatoid arthritis showed 60% of the participants developed rheumatoid arthritis within five years, or less. Mean values of maximal voluntary ventilation (MVV) was significantly lower than in the participants actual measures compared with the mean of predicted values**.** The mean values of both maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) were significantly lower than in participants' actual measures and predicted values. There was significant statistical relation between the maximal voluntary ventilation (MVV) and maximal expiratory pressure (MEP), maximal inspiratory pressure (MIP) of the participants**.** *Conclusion:* Maximum voluntary ventilation (MVV), maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) are essential parameters to evaluate the respiratory muscles strength among patients with rheumatoid arthritis. We may be recommended to be to perform these tests done routinely as a part of airflow category of pulmonary function testing for those patients as there are no adverse effects, non-invasive and relatively easy to perform manoeuvres.

Keywords: Expiratory pressure, Inspiratory pressure, Rheumatoid Arthritis, Voluntary ventilation

1. INTRODUCTION

Muscle endurance is defined as the ability to sustain a specific muscular action related to time. It emphasises the integrations and quality of the muscles with resistance to fatigue (American Thoracic Society/European Respiratory Society., 2002). Measurement of endurance is achieved specific manner because of the diversity of recruitment patterns of motor units and synergists among muscle groups with varying endurance qualities (American Thoracic Society/European Respiratory Society., 2002). Regarding respiratory muscles, ventilatory endurance testing aims to measure the maximum sustainable ventilation (MSV), as a fraction of maximal voluntary ventilation (MVV) (American Thoracic Society/European Respiratory Society., 2002). MVV is a detecting parameter for several pulmonary physiological aspects such as lung volume changes, respiratory muscle functioning, compliance of the thorax lung complex and airway resistance (Sheldon et al., 2000). MVV is referred to the maximum amount of air that a person can breathe over a specified period which is about 12 seconds for normal subjects (Millre et al., 2000). It can be used as a tool for assessment of respiratory muscle weakness (Gibson et al., 2002). Measurement of MVV is an essential step for interpretation of maximal MSV which is expressed as a fraction of MVV (Clanton et al., 2002).

In 1969 Hyatt and Black introduced a simple hand-held mouth pressure meter as a method to measure maximal respiratory pressures in cm H_2O (Black and Hyatt et al., 1969). Assessment of global respiratory muscle strength using maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) which are international measures of maximal strength of respiratory generated during maximal inspiration and expiration against a closed airway (Neder et al., 1999). MIP is an estimation of global inspiratory muscle strength with a close relationship with diaphragmatic strength, as it is the major inspiratory muscle while MEP is created by the abdominal and intercostal muscles (American Thoracic Society/European Respiratory Society., 2002). They widely used test to assess muscle pressures, as it has (American Thoracic Society/European Respiratory Society., 2002) and may be very useful in the diagnosis and follow-up of pulmonary and cardiac disease (Myers et al., 2005).

Respiratory muscle strength testing is forced manoeuvres take place during maximal spirometry efforts (Carl., 2019). MIP is the minimum pressure developed during a forceful and sustained inspiration against an occluded airway (Carl., 2019). Measurement is taken after a maximal expiration as near to residual volume, and recorded as a negative value in cm H2O or mm Hg (Carl., 2019). MEP is the maximal pressure that can be developed during a forceful and sustained expiratory effort against an occluded airway. It is usually measured after a maximal inspiration as near to total lung capacity, reported as a positive value in cm H_2O or mm Hg (Carl., 2019). Assessment and evaluation of the strength of the respiratory muscles is beneficial in clinical conditions, interpretations with

other airflow categories of pulmonary function testing and in an intensive care unit to wean from mechanical ventilation (Robert et al., 2014).

Rheumatoid arthritis (RA) is a chronic inflammatory condition of the musculoskeletal system with a clinical picture dominated by signs and symptoms of joint involvement (Smolen et al., 2016). RA is articular disorder with extra-articular manifestations (EAMs) affecting other organs and tissues lead to worsening prognosis. The incidence of EAMs is detected with variable results across different studies (Prete et al., 2011). EAMs develop in 18–40% of RA patients, while the incidence of severe EAMs ranges from 1 to 20% being the first presentation of the disease before any articular involvement (Prete et al., 2011). The involvement of the pulmonary system occurs in about 30–40% of RA patients (Fischer & du Bois, 2012). Pulmonary events in RA mainly reflect the involvement of interstitium, airways, and pleurae (Fischer & du Bois, 2012; Urisman & Jones, 2014). They have been recognised as the second most frequent cause of death in RA patients, after cardiovascular disease (Pinheiro et al., 2015).

In 2014, Almoallim published a review article about the condition of rheumatoid arthritis in Saudi Arabia concluded that RA in Saudi Arabia is the suboptimal and exact prevalence of RA among the Saudi population is undetectable (Almoallim et al., 2014). A study in Taif city had been conducted in 2015 of RA concluded that the prevalence was similar to the estimated on a global scale (Jamal Albishri et al., 2015). Respiratory system involvement is one of the commonest as EAMs in Saudi Arabia makes early recognition important to decrease mortality (Al-Ghamdi et al., 2009).

This research would provide information about respiratory muscles strength among asymptomatic patients with rheumatoid arthritis hence it would shape an insight about RA patients' respiratory workup by measuring of maximal voluntary ventilation, maximal expiratory pressure and maximal inspiratory pressure among the participants and correlate with the predicted values.

2. PATIENTS AND METHOD

Study design and Setting

It was analytical, facility-based study, conducted in the Pulmonary Function Test lab, Department of Respiratory Care, and the Outpatient Clinics of the Rheumatology Unit at the Department of Internal Medicine in King Saud Medical City (KSMC) which a government tertiary hospital is serving the people of Riyadh-KSA since 1956. The study duration was 4 months conducted from October 2019 to February 2020.

Patients and Sampling

A 70 Patients confirmed with rheumatoid arthritis, according to the American College of Rheumatology/European League against Rheumatism classification (Aletaha et al., 2010) were selected with age group 18-75years old. Patients confirmed with symptoms or chronic respiratory disease before Rheumatoid arthritis, pregnant ladies, obesity BMI more than 35; smoker patient and Non-Arabic non-English languages speakers were excluded. Consecutive sampling for any case who present with connective tissue disease until the sample is reached.

Pulmonary Function Tests Methods

MVV, MEP and MIP tests were carried out using spirometer MasterScreen PFT (CareFusion, Hoechberg Germany manufacture). The machine was calibrated daily. We used of the MicroGard ® mouthpieces containing filter to prevent the infections. Regarding MVV manoeuvre, just before starting the measurement, the patient closed the nose with the nose-clip, take the mouthpiece between the teeth and keep the lips tightly around the mouthpiece. The patient breathe normally at least five breaths were required. Then, the patient was instructed to inhale and exhale as fast immediately and as deeply as possible at least 12 seconds of maximal ventilation. The patient can continue to breathe normally again, and the measurement was ended. For MIP manoeuvre, just before starting the measurement, closed off the patient's nose with the nose-clip. The patients take the mouthpiece between the teeth and keep the lips tightly around the mouthpiece. Correct position of the mouthpiece checked. At the earliest after five breaths as tidal breathing, the patient was instructed to exhale deeply. Then, the patient was asked to breathe in as fast and strongly as possible against the closed shutter and to maintain the pressure for at least 2 seconds. For MEP manoeuvre, just before starting the measurement, close off the patient's nose with the nose-clip. The patient takes the mouthpiece between teeth and keep lips tightly around the mouthpiece. The correct position of the mouthpiece checked the patient was instructed to relax and breathe normally, at the earliest after five breaths as tidal breathing. Then the patient was instructed to inhale deeply after a deep inspiration, and the patient was asked to breathe out as fast and strongly as possible against the closed shutter and to maintain the pressure for at least 2 seconds. All the tests had met the acceptability and repeatability criteria according to American Thoracic Society (ATS) and European Respiratory Society (ERS) (Graham et al., 2019).

Questionnaire

Detailed structured, a questionnaire was filled for each respondent after explaining to them the study and its benefits. The questionnaire first was subjected to a probe of ten patients, modified and then used.

Data management and Analysis

Data was entered and analysed using Statistical Package for Social Sciences (SPSS), version 21. Variables were expressed by means and standard deviations (SD). Means comparing tests and Pearson correlation were used to compare the mean differences between the two groups. A value of $p<0.05$ were considered significant.

3. RESULTS

Demography of Participants

A total of 70 subjects in the age group 18-65 years participated in the study. 14.3% of the study participants were male subjects while 85.7%were female subjects. Saudis constituted 88.6% of the participants were Saudis and 12.4% non-Saudis. The distribution of the chronicity of rheumatoid arthritis showed 60 % of the participants developed rheumatoid arthritis within five years, or less. 15.7% of the participant started the spirometry maneuvers but did complete the tests.

Table 1: The Demographic distribution of the participants (N=70)

Gender		
Variables	**Frequency**	**Percentage**
Males	10	14.3 %
Females	60	85.7 %
Age Grouping		
Variables	**Frequency**	**Percentage**
18-25	2	2.9 %
26-35	5	7.1 %
36-45	21	30.0 %
46-55	26	37.1 %
56-65	9	12.9 %
above 65	7	10.0 %
Ethnicity		
Variables	**Frequency**	**Percentage**
Saudi	62	88.6 %
Non-Saudi	8	11.4 %
Chronicity of Rheumatoid arthritis		
Variables	**Frequency**	**Percentage**
Less than on year	7	10.0 %
1 year-5 years	35	50.0 %
6 years-10 years	11	15.7 %
11 years-15 years	7	10.0 %
16 years- 20 years	6	8.6 %
More than 20 years	4	5.7 %
Endurance to complete the tests		
Variables	**Frequency**	**Percentage**
Participants completed the tests	59	84 %
Participants did not complete the tests	11	15.7 %

In table 2, the results illustrate that the mean values of MVV is significantly lower than in the participants compared with the mean of predicted values.

Table 2: Descriptive analysis and the correlation between the participants actual measures and predicted values regarding maximal voluntary ventilation (MVV) (N=59)

		Minimum	Maximum	Mean ± Std. Deviation	P
Maximal Voluntary Ventilation L/min	Participants actual measures	4.06	146.05	61.01±24.48	.000*
	Predicted values	74.68	145.64	97.49±14.50	

*Significant at P<0.001

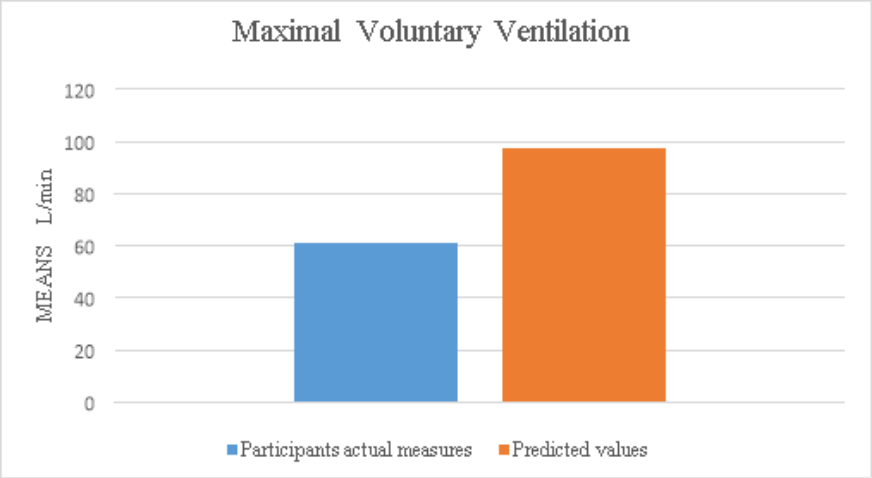

Figure 1: The means of participants actual measures and predicted values regarding maximal voluntary ventilation (n=59)

Regarding table 3 the results demonstrate the mean values of both MIP and MEP that are significantly lower than in the participants compared with the mean of predicted values.

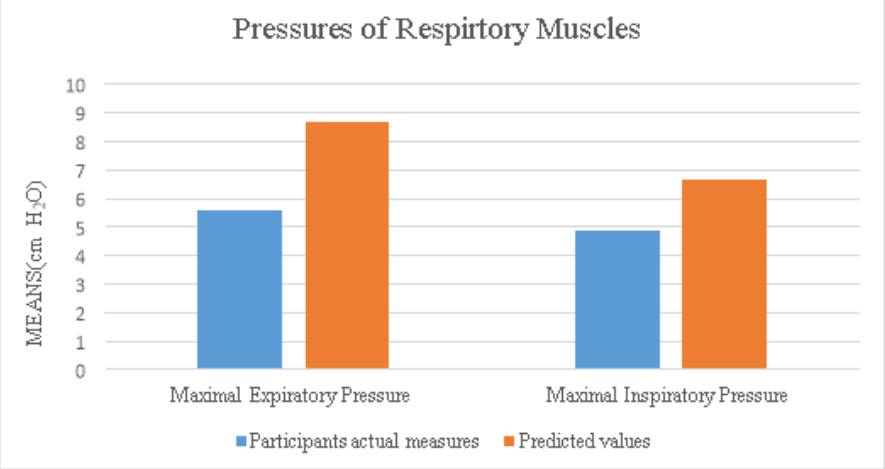

Figure 2: The means of participants actual measures and predicted values regarding maximal expiratory pressure and maximal inspiratory pressure (n=59)

Table 3: Descriptive analysis and the correlation between the participants actual measures and predicted values of maximal expiratory pressure (MEP) and maximal inspiratory pressure (MIP) (N=59)

		Minimum	Maximum	Mean ± Std. Deviation)	P
Maximal Expiratory Pressure (cm H_2O)	Participants actual measures	.16	14.86	5.58±2.61	.000*
	Predicted values	6.06	14.47	8.69±2.36	
Maximal Inspiratory Pressure (cm H_2O)	Participants actual measures	.33	13.01	4.88±2.77	.000*
	Predicted values	4.89	10.43	6.65±1.32	

*Significant at P<0.001

In table 4 the analysis of the result interprets the presence of a statistical relationships between maximal voluntary ventilation (MVV) and maximal expiratory pressure (MEP), maximal inspiratory pressure (MIP).

Table 4: Correlations between the maximal voluntary ventilation (MVV) and maximal expiratory pressure (MEP), maximal inspiratory pressure (MIP) of the participants (N=59)

		Maximal Expiratory Pressure (MEP)	**Maximal Inspiratory Pressure (MIP)**
Maximal Voluntary Ventilation (MVV)	Significance	**.007***	**.001***
	Pearson Correlation	0.346	0.419

*Significant at P<0.05

4. DISCUSSION

Direct measurement of respiratory muscle strength can be done by measuring MIP and MEP as they may be more sensitive in evaluating respiratory muscle dysfunction in early stage compared with slow and forced spirometry (Evans & Whitelaw, 2009). Our results showed that the mean values of MVV were significantly lower than in the participants compared with the mean of predicted values. our result match with a study conducted by Xu Yinghui et al. 2004 in China evaluate the changes of lung function in patients with rheumatoid arthritis. Among 20 RA patients and 20 normal and showed lung function impairment, including MVV were decreased compared with normal subjects (Xu Yinghui et al., 2004). Another study was done in India, among 40 normal control group in the age group between 25-55 years and 40 patients with RA and the results showed statistically significantly reduced pulmonary function parameters including MVV (Jeyakumar, 2018). Our results showed that the mean values of both MIP and MEP were significantly lower than in the participants compared with the mean of predicted values with significant statistical relation between the MVV and MEP, MIP of the participants. Çimen et al., (2001) investigated patients with rheumatoid arthritis through MVV, MEP, MIP and cardio-respiratory exercise tests to evaluate the respiratory involvement, inspiratory and expiratory muscle strength and endurance, they found that RA patients have normal pulmonary function tests but reduced respiratory muscle strength and endurance, and also reduced aerobic capacity compared to controls. According to this result, it may be recommended respiratory and aerobic exercises to improve respiratory muscle strength and endurance (Abdelbasset et al. 2020; Zade et al. 2020). Our results also matched with a study conducted in juvenile chronic arthritis to determining lung function and disability in 31 children and concluded that impairment was found in respiratory muscle strength in children with systemic and juvenile chronic arthritis (Knook et al., 1999). Gorini et al., (1990) evaluated inspiratory muscle strength by MIP among 15 patients with rheumatoid arthritis RA and in 12 age they noticed a significant inverse relationship in the patients between maximal inspiratory pressure MIP and duration of steroid therapy.

Our result revealed that about 15.7% of the participant started the spirometry maneuvers but did not tolerate the test because they were unable to follow directions. It's one of the reasons suggested by Jack Wagner (2012) concluded that acceptable and repeatable results obtained from spirometry is not an easy task.

5. CONCLUSION

MVV, MIP and MEP are essential parameters to evaluate the respiratory muscles strength among patients with rheumatoid arthritis. We may recommend performing these tests done routinely as a part airflow category of pulmonary function testing for those patients as there are no adverse effects, non-invasive and relatively easy to perform maneuvers.

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Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval for human

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Review-Research Center-KSMC, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards (ethical approval number H1RE-18-Jul19-01). The study was approved by the Local Ethics Committee Board numbered (1/191) - Almaarefa University.

Conflict of Interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are available upon request to the corresponding author.

Peer-review

External peer-review was done through double-blind method.

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