THE USE OF BIOMARKERS TO PREDICT ATTACKS OF SEVERE BRONCHIAL ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Introduction: Increased levels of C-reactive protein (CRP) and fibrinogen among asthmatic and Chronic Obstructive Pulmonary Disease (COPD) patients were associated with disease severity and complications.

Aim of the work: To assess the possible relationship between selected variables and hospitalization as unfavorable outcome.

Subjects and methods: 172 subjects had participated in this observational study and grouped into three groups; control, asthmatic and COPD. Blood analysis used for fibrinogen and CRP levels and pulmonary function were measured. Statistical analysis using t-test, ROC, and regression test in order to assess the predictive potential of those variables.

Results: mean of fibrinogen among COPD group (583.24 mg/dL) was significantly higher than control (207 mg/dL), (P<0. 001). Mean of CRP (14.2 mg/L) was significantly higher than control (0.98 mg/L), (P<0.001). Mean of fibrinogen among asthmatic group (414.8 mg/dL) was significantly higher than control (207 mg/dL). Mean of CRP (10.2 mg/L) was significantly higher than control (0.98 mg/dL). Statistically significant inverse correlation was found between fibrinogen and ratio of Forced Expiratory Volume in the first second (FEV1) to full Forced Vital Capacity (FVC) this ratio is expressed as FEV% (r=-0.885). Also, an inverse correlation between CRP and FEV% (r=-.75). ROC analysis suggested cut score for fibrinogen at 445 mg/dL, 370 mg/dL for COPD and asthmatic groups respectively, while CRP

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at 9.4 mg/L, 7.25 mg/L for COPD and asthmatic groups respectively. Regression analysis explained that 43% of causes for hospitalization might be for level variation of fibrinogen and CRP.
Conclusion: increased levels of fibrinogen and CRP might be associated to increased risk of hospitalization.
Keywords: Asthma, COPD, CRP, Fibrinogen.

INTRODUCTION

Asthma and Chronic obstructive pulmonary disease both possess the highest prevalence rate among lung disease. In 2019, COPD ranked as third cause of death around the globe, while asthma is diagnosed among 262 million people in the same year (WHO, 2021). In addition, both are chronic disease that might have unfavorable consequences regarding quality of life and disease burden. Hospitalization is considered as one of the most unfavorable outcomes that the patient could have because it has an economical burden for the patient and creates a psychological distress (Ehteshami *et al.*, 2016). Therefore, the need for a predictive biomarker that might provide an estimation regarding the possibility of hospitalization is in need (Mannino *et al.*, 2015). A reliable biomarker might be used as guideline for the physician to modify or change the therapeutic treatment (Cazzola & Novelli, 2010). There are numerous studies that suggest the possibility of using fibrinogen, CRP and pulmonary function as predictive biomarkers (Mannino *et al*., 2015). Predictive markers have a positive outcome in treatment of asthma condition particularly severe asthma (Tiotiu A., 2018).

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C**hronic Pulmonary Disease and Asthma**: Asthma is ranked in the 16th place as major cause of years that are lived with disability; besides, it holds the 28th place of disease burden with about 300 million of asthmatic people worldwide, about half of them live in developing countries (Dharmage *et al*., 2019). In addition, asthma is responsible for direct and indirect cost for patient, family and government. To illustrate, asthma cost about 3000 USD for each patient in United States, while in European countries the total cost is about 20 billion Euros (Nurmagambetov *et al*., 2018). In Egypt, asthma prevalence is about 7% (Mungan *et al*, 2018). Similarly, COPD has a significant economic burden. For example, in Europe, COPD consume about 6% of health care budget (Buja *et al*., 2020). In US, COPD cost 32 billion USD in the year 2010, and estimated to increase with 10 billion more in 2020 (CDC, 2018).

In Egypt, about 10% of population might suffer from COPD (Said *et al*., 2015). The economic burden is notable either for patient, family or health care system; in addition, any further complication might lead to hospital admission that causes a more burden.

Biomarkers: Biomarkers are considered as an indicator that is used to assess the severity and intensity of the diseases; besides, biomarkers help the physician to predict and assess the outcome of therapeutic treatment or to avoid undesirable consequences. Also, biomarkers might be associated with the risk or disease progression (FNIH, 2015). According to Težak *et al*. (2010), biomarkers are vital for medical biology that help in early diagnoses

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and risk prevention. Biomarkers provide leverage for better treatment and symptoms control; therefore, the physician might have more control over symptoms and improve the therapeutic outcome (Pritzker, 2012).

Biomarkers might be specific cells, molecules, genes, byproducts, metabolites, enzymes or hormones; in addition to, an organ function or changes in biological or physiological properties. Biomarkers can be identified as a measurement for molecular or biological criteria in different body organs or in the blood sample. Biomarkers are used long time before; however, in current time, biomarkers are become more developed and intertwined (FNIH, 2015)

Fibriongen and C reactive Protein: Fibrinogen is a blood clotting factor that is released in a response to the stimulation of interleukin six (Gabay and Kushner, 2000). Fibrinogen levels are notably higher in COPD patients with frequent exacerbations and used to hospital admission and emergency room visits (Duvoix *et al.*, 2013).

C Reactive Protein (CRP) is a marker of inflammation and knowns as first acute phase protein, and it is sensitive to inflammation, tissue damage and infection (Olafsdottir *et al.*, 2005). Despite that the CRP is not a specific marker for a respiratory outcome, it is notably higher in hospitalized asthmatic (Monadi *et al*., 2016), and COPD patients are also show a higher CRP during hospitalization or attending emergency room (Mannino *et al.*, 2015). According to many studies, fibrinogen and CRP might be used as a

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promising biomarker to monitor asthma and CODP (Cazzola & Novelli, 2010).

AIM OF STUDY

To evaluate the possible relation between level of fibrinogen, CRP and hospitalization which can be used to determine a possible hospitalization risk for both asthmatic and COPD patients.

METHODS

Fibrinogen and CRP levels were measured in COPD, asthmatic and control subjects with total of 172 subjects who were reviewed at the outpatient clinic at Ahmed Maher hospital in Alexandria between April 2019 till April 2021. Asthmatic patients were chosen according to GINA 2019 Global Initiative For Asthma, while COPD patients were selected and severity were categorized according to GOLD 2019 Global Initiative For Chronic Obstructive Lung, Other eligible criteria included at least one hospitalization or two visits to the clinic or emergency department during the previous six months and the age of both sexes should be from 40 to 65 years old. Exclusion criteria include extremely severe cases of asthmatic and COPD. Severe asthma cases that are prescribed step 5 medication such using anti immunoglobulin E or interleukin- 4R as a treatment (GINA 2019), while very sever COPD patients are classified as GOLD 4 with FEV% < 30% (GOLD 2019).

A baseline clinical evaluation included questionnaire The Saint Georg questionnaire (Jones *et al*, 1991) on complications related to asthma and COPD. The questioner was validated for Egyptian culture (Metwally, 2004). Pulmonary function test was assessed through spirometer device and performed by expert physician. Subjects were divided into three groups. Group (1) included 58 control subjects, group (2) included 65 asthmatic patients, and group (3) included 49 COPD patients. A blood sample was taken to measure the level of CRP and Fibrinogen. A record was taken for patients whose condition required a hospitalization or Emergency Room (ER) admission after clinical examination.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS software V.20. Descriptive statistic includes simple measures such as mean, median and standard deviation from sample population, while inferential statistics include independent sample t-test, and relationship test. Sample t-test used to compare means among group subjects. Relationship test include correlation coefficient test to reveal if there is a relation among variables and outcome. Selected variables were c reactive protein and fibrinogen levels, while selected outcome was hospitalization. In addition, regression analysis, analysis of variance test (ANOVA) and ROC was performed in order to investigate the significance of each variable, and to assess a possible cut off point for the selected variables.

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Questionnaire: Questionnaires were filled out by subjects under interviewer supervision. The questionnaire included information about socio-economic status, age, exposure to risk factors such as tobacco smoke, inhaling for irritant or exposure to harmful occupational substance such as asbestos, An Arabic version of the questionnaire was used that are validated by Metwally, (2004).

Blood Sample and Pulmonary Function Tests: Pulmonary function test was done for all subjects using spirometer. After that, a blood sample had withdrawn for analysis of Fibrinogen, CRP and CBC. CRP used agglutination assay method using ASI CRP LATEX kites using saline for dilution. An Enzyme-Linked immunosorbent Assay (ELISA) were used to measure Fibrinogen.

RESUTLS

A total of 172 subjects were screened for possible enrollment between April 2019 and April 2021. Subjects were divided into three groups control, asthmatic and COPD. There were 58 control subjects in Group (1), there were 65 asthmatic subjects in Group (2), and there were 49 COPD subjects in Group (3). The control subjects were subjects that visits outpatient clinic for different reasons of non-respiratory problem, while COPD and asthmatic subjects were at stable state and used to visit the outpatient clinic in order to follow up their disease condition and to have their medical prescription. In group 1, 34.5% subjects were current smoker, while 10.4% were previous

smokers. In group 2, only 26.2% subjects were current smoker, and 24.6% were previous smokers. In group 3, only 10.2% were current smokers, while 71.4% were previous smokers. The mean age for control group was 48 years, and the mean age for the asthmatic group was 44.8 years, while the COPD group showed the highest age mean with 58 years. About 13.3% of all subjects reported that they had a cardiovascular disease, and suffered from atherosclerosis, while about 7.6% of all subjects were reported diabetic. Characteristics of control, asthmatic and COPD group are illustrated in Table (1).

Table (1): Characteristics of Control, Asthmatic and COPD groups

	Patients with		
	Control	**Asthma**	**COPD**
	N = 58	N= 65	N= 49
Age, years	48.7±0.93	44.8±1.4	58.4±1.13
Males	28 (48%)	38 (58.5%)	37 (75.5%)
Female	30 (52%)	27 (41.5%)	12 (24.5%)
Smoking status			
Current smokers	20 (34.5%)	17 (26.2%)	5 (10.2%)
Previous smokers	6 (10.4%)	16 (24.6%)	35 (71.4%)
Never smoked	32 (55.2%)	32 (49.2%)	9 (18.4%)
Body Mass Index	25.47±3.4	23.17±3.2	20.75±1.7
Ratio of FEV1/FVC (FEV%)			
FEV%	97.37%± 6.1	75.9%±10.2	56.16%±5.66
Other Disease			
Cardiovascular disease (13.3%)	4 (6.9%)	3 (4.6%)	16 (32%)
Diabetes mellitus (7.6%)	10 (17.2%)	1 (1.5%)	2 (4%)
Atherosclerosis (13.3%)	13 (22.4%)	7 (10.7%)	4 (8%)

COPD: Chronic Obstructive Pulmonary disease. BMI: Body Mass Index. FEV% is the Ratio of FEV1/FVC (Velez *et al*, 2017). FEV1: Forced Expiratory Volume in the first second of expiration, FVC: Forced Vital Capacity.

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CODP group showed the highest mean age with 58.4 years comparing to control and asthmatic groups with 48.7 and 44.8 years respectively. Males were 75.5%, COPD group while males in asthmatic group were 58.5%. Control group was almost having equal distribution of both sexes. Nearly half of control group (1) 55.2% and asthmatic group (2) 49.2% were never smoked before, while 18% of COPD group (3) never smoked. Regarding Body Mass Index BMI, COPD group showed the leanest subjects with mean of 20.76, while asthmatic group and control group has 23.17 and 25.47. COPD group showed the lowest mean of FEV%, then asthma group and control group, 56.16%, 75.9% and 97.37% respectively.

Table (2): Fibrinogen and CRP levels in Control, Asthmatic and COPD group

Inflammatory marker		**Group**	
	Control	**Asthma**	**COPD**
	N = 58	N = 65	N = 49
CRP (mg/L)	0.98 ± 0.15	10.2 ± 5.9	14.2 ± 6.7
Fibrinogen (mg/dL)	207.3±34	414.8± 160.2	583.24 ± 70.2
Ratio of FEV1/FVC (FEV %)	97.37% ± 6.1	75.9% ± 10.2	56.16%±5.66

COPD: Chronic Obstructive Pulmonary disease. FEV% is the Ratio of FEV1/FVC (Velez *et al*, 2017). FEV1: Forced Expiratory Volume in the first second of expiration, FVC: Forced Vital Capacity.

The highest mean of Fibrinogen (583.24 mg/dL) were detected among COPD group, then, followed by asthmatic group with a mean of (414.8 mg/dL), while control group has a normal mean of fibrinogen (207.3 mg/dL). Mean of CRP has the highest value among COPD group (14.2 mg/L),

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followed by asthmatic group with (10.2 mg/L), while control group shows normal mean with (0.98 mg/L). COPD has the lowest mean of FEV%, then asthma group and control group, 56.16%, 75.9% and 97.37% respectively.

Table (3): Comparison of the mean of CRP and fibrinogen in control and COPD group and asthmatic group

Inflammatory marker	**Group**				
	Control	**Asthma**		**COPD**	
	N = 58	N = 65	P-Value	N =49	P-Value
CRP (mg/L)	0.98±0.15	10.2± 5.9	≤ 0.001	14.2 ±6.7	≤ 0.001
Fibrinogen (mg/dL)	207.3±34	414.8± 160.2	≤ 0.001	583.24 ±70.2	≤ 0.05
FEV%	97.37%±6.1	75.9%±10.2	≤ 0.001	56.16%±5.66	≤ 0.001

COPD: Chronic Obstructive Pulmonary disease. CRP: C Reactive Protein. FEV% is the Ratio of FEV1/FVC (Velez *et al*, 2017). FEV1: Forced Expiratory Volume in the first second of expiration, FVC: Forced Vital Capacity.

COPD group was significantly different from control group in CRP (P-Value ≤ 0.001), fibrinogen (P-value ≤ 0.05) and FEV% (P-Value≤ 0.001). Asthmatic group was significantly different from control group in CRP (P-Value ≤ 0.001), fibrinogen (P-value ≤ 0.001) and FEV% (P-value ≤ 0.001).

Table (4): Correlation between Fibrinogen, CRP and FEV%

Correlation between fibrinogen and CRP	r = 0.456
Correlation between CRP and FEV%	r = - 0.75
Correlation between Fibrinogen and FEV%	r = - 0.885

CRP: C Reactive Protein. FEV% is the Ratio of FEV1/FVC (Velez *et al*, 2017). FEV1: Forced Expiratory Volume in the first second of expiration, FVC: Forced Vital Capacity.

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A strong invers correlation is detected between C Reactive Protein, fibrinogen and FEV % with r = - 0.75, and r = - 0.885 respectively. A moderate correlation between fibrinogen and CRP is detected with r = 0.456.

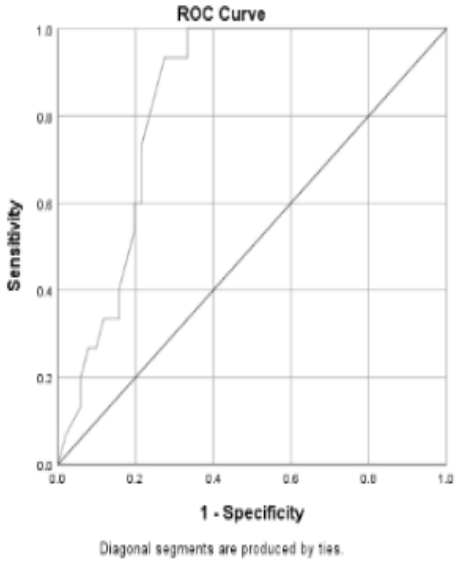

Figure (1): Fibrinogen ROC curve for Control and COPD group

Figure (1) illustrates an area under the curve with 0.755, and sig = 0.001. The suggested cut score for fibrinogen is 445 mg/dL. As AUC is between 0.75 and 0.85, thus AUC shows a moderate accuracy and about 75.5% chances that the value ≥ 445 mg/dL of fibrinogen might show risk of hospitalization.

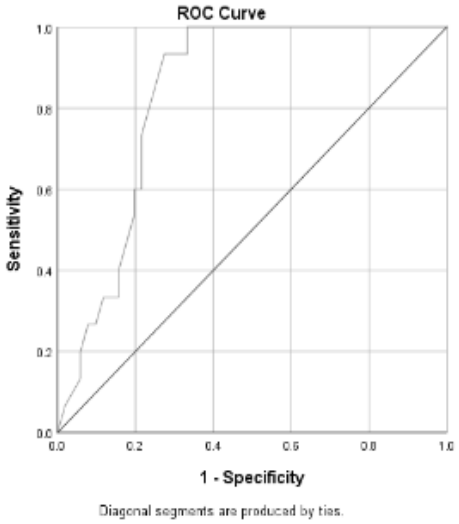

Figure (2): C Reactive Protein ROC curve for control and COPD group

Figure (2) illustrates an area under the curve with 0.72, and sig = 0.001. The suggested cut score for CRP is 9.4 mg/L. As AUC is less than 0.75, thus AUC shows a low accuracy and about 72% chances that the value ≥ 9.4 mg/L of C reactive protein might show a risk of hospitalization.

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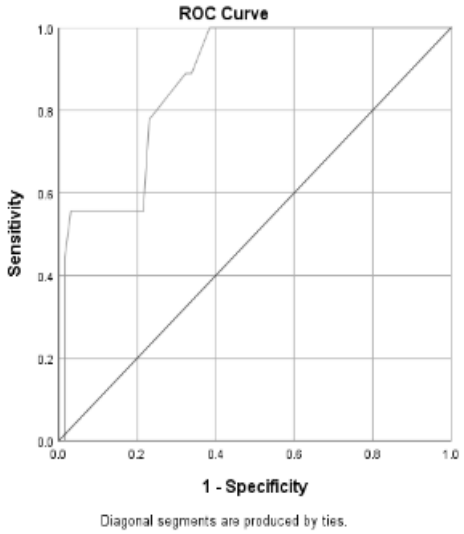

Figure (3): Fibrinogen ROC curve for Control and asthmatic group

Figure (3) illustrates an area under the curve with 0.66, and sig = 0.001. The suggested cut score for fibrinogen is 370 mg/dL. As AUC is less than 0.70, thus AUC shows a low accuracy and about 66% chances that value ≥ 370 mg/dL of fibrinogen might show a risk of hospitalization.

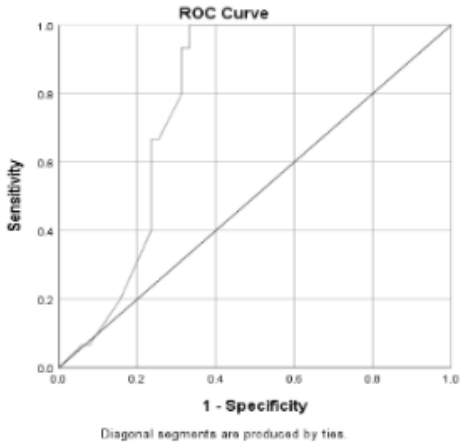

Figure (4): C Reactive Protein ROC curve for control and asthmatic group

Figure (4) illustrates an area under the curve with 0.76, and sig = 0.001, and the suggested cut score for CRP is 7.25 mg/L. As AUC is more than 0.75 and less than 0.85, thus AUC shows a low accuracy and about 76% chances that the value ≥ 7.25 mg/L of CRP might show a risk of hospitalization.

Linear Regression Statistics:

Table (5): Model summary table

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0.657[a]	0.432	0.414	1.23212

From table (5), R-square is = 0.432. That is mean that about 43% causes of hospitalization risk are due to variation of fibrinogen, CRP levels and

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pulmonary function measurement, while there is other 56% reasons contributed in risk of hospitalization.

Table (6): ANOVA Table

ANOVA						
Model		Sum of Squares	Df	Mean Square	F	Sig.
1	Regression	113.068	3	37.689	24.826	0.0001[b]
	Residual	148.775	98	1.518		
	Total	261.843	101			

From table (6) the ANOVA table, sig = 0.0001, thus the model is significant and we can use the model that have variable of fibrinogen, CRP and pulmonary function and hospitalization as an outcome.

Table (7): Co-efficient Table

Co-efficient						
Model		Unstandardized Coefficients		Standardized Coefficients	T	Sig.
		B	Std. Error	Beta		
1	(Constant)	-0.474	2.969		-0.160	0.004
	Fibrinogen	0.04	0.002	0.413	1.786	0.0001
	CRP	0.049	0.037	0.217	1.311	0.009
	FEV%	-0.09	0.024	-0.113	-.357	0.0001

From Table (7), the included variables have a significant effect upon hospitalization. From coefficient table, we can conclude the regression equation is Hospitalization =

-0.474 + 0.04 (Fibrinogen) + 0.049 (CRP) + -0.09 (FEV %).

From the equation, 0.04 shows how fibrinogen will affect hospitalization, since the value is positive, thus when fibrinogen increases by one unit, hospitalization will increase by 0.04. From the equation, 0.049 shows how CRP will affect hospitalization, since the value is positive, thus when CRP increases by one unit, hospitalization will increase by 0.049. Regarding FEV%, since the value is negative, therefore when FEV% value is decreased by one unit, the hospitalization will increase by 0.09.

DISCUSSION

Asthma and COPD both causes a serious dieses burden around the globe with a notable economic burden, and that burden could be increased in case of hospital admission. Using reliable biomarkers that provide a clearer interpretation for the disease severity and condition might help the physician to provide a better treatment plan and avoid unfavorable consequence; however, biomarkers that predict asthma and COPD severity are still in early beginning (Duvoix *et al*., 2013). This study evaluates if fibrinogen and CRP have a predictive potential of possible hospitalization for COPD and asthmatic patients.

The current study found that fibrinogen mean was 414.8±160.2 mg/dL in asthmatic group which was significantly higher than mean level of fibrinogen in control group (P-value ≤ 0.001). That finding agrees with Higashimoto *et al*., 2008. Another finding revealed that asthmatic patients is significantly

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having higher fibrinogen level with 477 mg/dL (P <0.007) (AL-Aaraji *et al*., 2019).

In COPD group, fibrinogen mean was 583.24±70 mg/dL, which was significantly higher than control group (P-value ≤ 0.001) which agreed with a cohort study conducted by Mannino *et al*., 2015. In asthmatic group, CRP mean was 10.2 mg/L and significantly higher than control group (P < 0.05) which agreed with findings of Obaidi *et al*., 2010. In COPD group, CRP mean was 14.2 mg/L, which was significantly higher than control group which agreed with finding of Fattouh & Alkady, (2014). A similar findings of Thomsen *et al* and Aksu *et al*., 2013 supports that CRP level is significantly higher in COPD.

By using person coefficient, a moderate correlation between fibrinogen levels and CRP levels r = 0.456 was found; however, there was a strong inverse correlation between FEV% and CRP (r= -0.75). Similarly, FEV% showed a strong inverse relation with fibrinogen (r = -0.885). A similar inverse correlation among COPD patients were observed in study of Fattouh & Alkady, (2014).

In order to find a cut off score for fibrinogen level among COPD patients, a ROC curve was used for fibrinogen values of control and COPD group. The AUC was 0.786 and the suggested point was 445 mg/dl with 78.4% sensitivity and 27.3% specificity that is relativity agreed with study of Mannino *et al*., (2015). According to Mannino *et al*., (2015), COPD patient with fibrinogen level is equal or higher than 350 mg/dL might be associated

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with increased risk of hospitalization and worsen of exacerbations. Another study conducted by Valvi *et al.*, (2012) revealed that COPD patient with more than 390 mg/dL of fibrinogen will have higher chances of admitting to hospital. According to Dahl *et al.*, (2007) Relative risk of hospitalization if levels of fibrinogen are more than 378 mg/ml is 2.5% with 8.5% odd ratio. Another study suggests a nearly relative risk for hospitalization of 1.7%.

In order to find a cut off score for CRP level among COPD patients, a ROC curve was used for CRP value of control and COPD group. The AUC was 0.72 and the suggested CRP cut off score is 9.4 mg/L with sensitivity 60% and specificity of 22.7%. According to Fattouh & Alkady, (2014), CRP levels more than 12.7 mg/ml is associated with hospitalization risk, and that findings agrees with Pahuja *et al.*, (2016) that found that CRP levels more than 17.5 mg/dL were associated with intensive care admission.

In order to find a cut off score for fibrinogen level among asthmatic group, a ROC curve was used for fibrinogen values of control and asthmatic group. The AUC was 0.66 and the suggested point was 370 mg/dl with 71.4% sensitivity and 28% specificity. Sprio *et al.*, (2020) had revealed a similar finding that suggested a fibrinogen level greater than 361mg/dL might have eight times risk of hospitalization than normal value. In order to find a cut off score for CRP level among asthmatic patients, a similar ROC curve was used for CRP value of control and asthmatic group. The AUC was 0.76 the suggested cut off score is 7.25 mg/ml with sensitivity of 88% and specificity

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29%. A similar study conducted by Gallego *et al.*, (2016) suggested that 10 mg/ml of CRP might be increase the risk of hospitalization by four times.

One limitation of this study is the use of two inflammatory biomarkers fibrinogen and CRP. Many studies suggest that the use of more than biomarkers such as IL-6, TGf-B1, tumor necrosis factor or other anti-inflammatory cytokines might provide more solid evaluation (Higashimoto *et al.*, 2008). The reason for selecting fibrinogen and CRP as biomarkers is that they are more convenient and inexpensive. Another limitation for the study is that the sample size might be small and need to include more subjects in order to strength the statistical results.

CONCLUSION AND RECOMMENDATION

The study revealed that the increased levels of CRP and fibrinogen in asthmatic and COPD patients might be associated with increased risk of hospitalization and exacerbation risk. Therefore, those two inflammatory biomarkers might have a promising potential for a predictive biomarker.

Future investigation that will include different types of biomarkers in order evaluated their potential. In addition, larger sample most likely will strength the statistical outcome.

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استخدام المؤشرات الحيوية للتنبؤ بنوبات الربو الشعبي الشديدة ومرض الإنسداد الرئوي المزمن

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المستخلص

ارتبطت زيادة مستوى البروتين التفاعلي والفيبرينوجين بين مرضى الربو ومرض الانسداد الرئوي المزمن مع شدة المرض ومضاعفات المرض. تم إجراء هذه الدراسة من أجل تقييم ما إذا كانت هناك علاقة بين تلك المتغيرات المختارة والدخول الي المستشفيات او قسم الطوارئ بغرض تخفيف الازمات الربوية. قد يكشف هذا التقييم عن معلومات حول جدوى استخدام هذه المتغيرات كمؤشرات حيوية

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تنبؤية لتوفير تحكم اكبر تجاه تلك الأزمات الربوية. التحق مائة واثنين وسبعين شخصًا في هذه الدراسة القائمة على الملاحظة وتم توزيعهم الي ثلاث مجموعات؛ مجموعة ضابطة ومجموعة مرضي الربو ومجموعة مرض الانسداد الرئوي المزمن. تم إجراء تحليل الدم لمستويات الفيبرينوجين والبروتين التفاعلي وقياس وظائف الرئة. ثم إجراء تحليل إحصائي للبيانات التي تم جمعها باستخدام اختبار العينة الواحدة ومنحني خصائص المستلم والمساحة تحت المنحي، واختبار الانحدار المتعدد من أجل تقييم الإمكانات التنبؤية لتلك المتغيرات المختارة. في مجموعة مرض الانسداد الرئوي المزمن، كان متوسط مستوى الفيبرينوجين (٥٨٣,٢٤ مجم / ديسيلتر) أعلى بكثير من المجموعة الضابطة (٢٠٧مجم / ديسيلتر)، أيضًا كان مستوى البروتين التفاعلي (١٤,٢ مجم / لتر) أعلى بكثير من مستوى المجموعة الضابطة (٠,٩٨ مجم / لتر). وبالمثل، كان متوسط مستوى الفيبرينوجين للمجموعة المصابة بالربو (٤١٤,٨ مجم / ديسيلتر) أعلى بكثير من المجموعة الضابطة (٢٠٧ مجم/ديسيلتر). أيضًا، كان مستوى البروتين التفاعلي (١٠,٢ مجم / لتر) أعلى بكثير من الضابطة (٠,٩٨ مجم /لتر). تم إجراء تحليل ومنحني خصائص المستلم والمساحة تحت المنحي وكانت نقطة القطع المقترحة للفيبرينوجين ٤٤٥ مجم / ديسيلتر ، ٣٧٠ مجم / ديسيلتر لمرض الانسداد الرئوي المزمن ومجموعة الربو على التوالي، في حين كانت نقطة القطع للبروتين التفاعلي ٩,٤ مجم / لتر ، ٧,٢٥مجم / لتر لمرض الانسداد الرئوي المزمن ومجموعة الربو على التوالي.

كشفت الدراسة عن وجود علاقة ذات دلالة معنوية بين الفيبرينوجين والبروتين التفاعلي ونسبة ووضائف التنفس. كمل توضح إحصائيات الانحدار الخطي أن ٤٣٪ من أسباب دخول المستشفي وأقسام الطوارئ قد تكون بسبب التغيرات في مستويات الفيبرينوجين والبروتين التفاعلي. وفي الختام، قد تترافق زيادة مستويات الفيبرينوجين ومع زيادة خطر الدخول الي المستشفي وأقسام الطوارئ لمرضي الربو والإنسداد الرئوي المزمن.