

RESEARCH

Relationship Between Serum IgE Level and Anxiety, Depression, Somatization and Quality of Life in Pediatric Asthma

Pediatric Astımda Kaygı, Depresyon, Somatizasyon ve Yaşam Kalitesi ile Serum IgE Düzeyi İlişkisi

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Abstract

The main purpose of the current study is to explore the potential relationship of asthma with depression, somatic predisposition, quality of life, manifest anxiety and Serum levels of IgE level. 141 participants between 6 and 12 years old were recruited and the following scales were used: Child Depression Inventory, Revised Version of Child Manifest Anxiety Scale, Pediatric Asthma Quality of Life Questionnaire and the Somatic Complaints Subscale of Child Behavior Check List. Based on asthma control level, severity of asthma was assessed by the specialists and the serum levels of IgE were assessed by using ELISA technique. The results indicated that there was a highly correlated relationship between serum levels of IgE and manifest anxiety levels among uncontrolled asthma group. These results suggested that, since the strong correlational relationship between the serum levels of IgE and manifest anxiety would have an effect on asthma control, future research should focus on this relationship from the aspect of psychoneuroimmunology.

Keywords: Asthma, pediatric asthma, IgE, mental health symptoms.

Öz

Bu çalışmanın amacı çocuklarda astım şiddeti ile depresyon, açık kaygı, yaşam kalitesi, somatizasyon gibi değişkenleri ve astımda bağışıklık sistemi belirleyicilerinden olan IgE düzeyi arasındaki olası ilişkiyi analiz etmektir. Toplamda 141 katılımcının bulunduğu bu çalışmanın örneklemini 6-12 yaş arası astımlı çocuklar oluşturmaktadır. Katılımcıların ruh sağlığı belirtilerini değerlendirmek adına Çocuk Depresyon Ölçeği, Çocuklar İçin Açık Kaygı Ölçeği, Pediatric Astımda Yaşam Kalitesi Ölçeği ve Davranış Değerlendirme Ölçeğinin Somatik Yakınmalar Alt Ölçeği kullanılmıştır. Astım şiddeti, astım kontrol düzeyi üzerinden uzman hekimlerce değerlendirilirken, Serum IgE düzeyleri ELISA tekniği kullanılarak elde edilmiştir. Kontrolsüz astım grubunda bulunan katılımcıların açık kaygı puanlarıyla IgE düzeyleri arasında orta düzeyde anlamlı yüksek korelasyon olduğu görülmüştür. Araştırma verileri değerlendirildiğinde, ruh sağlığı değişkenlerinden açık kaygı ile astımda bağışıklık sistemi belirleyicilerinden olan IgE düzeyi arasındaki ilişkinin, astım hastalığının şiddeti üzerinde etkili olabileceği yönünde veriler elde edildiğinden, gelecek araştırmaların söz konusu ilişkiyi psikonöroimmunolojik açıdan derinlemesine incelemesi önerilmektedir.

Anahtar sözcükler: Astım, çocukluk çağı astımı, IgE, ruhsal belirtiler.

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ASTHMA is one of the chronic diseases that can be commonly observed during childhood. Since asthma is a chronic disease which limits the mobility of individuals, as a frequently observed disorder (particularly within the stages of childhood) and reduces their quality of life further during winter; it may also affect children in socio-emotional aspect in addition to its physical effects. Over the 20th century, asthma has been one of the most studied chronic diseases in world health literature (Hossny et al. 2017). A considerable amount of these works have focused on the main effective and precipitating factors on asthma.

In light of the research conducted on the immunological circumstances of patients with asthma, it was noted that the majority of these studies have focused predominantly on the allergens and release of IgE. The literature has reported that allergens interact primarily with IgE and affect the clinical picture of asthma via IgE parameter (Burrows et al. 1988, Sears et al. 1991, Mills 2001). Specifically, Lupinek et al. (2017) suggested that there is a strong correlation between Serum IgE and allergic asthma complaints. However, despite the studies showing a strong correlation between asthma and IgE, there are also studies which found these variables insignificantly correlated. More specifically, Sandeep et al (2010) reported that IgE level increases occasionally as the severity of asthma increases; while this correlation was not statistically significant. When taking these results into account, it can be argued that the scientific literature is not consistent in dealing with the relationship between asthma and Serum levels of IgE and suggests other associations (moderator/mediator) between asthma and IgE.

Literature showed that a large number of studies that focused on the role of IgE in asthma also demonstrated that Th2 cells affect the synthesis of IgE (Barnes 1999). Specifically, Steinke and Borish (2001) mentioned that IL-4 had a specific role in the pathogenesis of asthma and noted that these cytokines synthesized IgE and consequently regulated allergic inflammation by Th2-cell differentiation. In the light of this, the roles of Th2 cells and IL-4 as well as IgE present as prominent.

On the other hand, studies on Th1 and Th2 cells from T-lymphocyte groups which play important roles in the pathophysiology of asthma also focus on the relationship between these cells and mental health. For example; Murali et al. (2007) noted that more than 300 studies have aimed to examine the association between stress and the Th1 and Th2 lymphocytes and specified that stress demonstrated a negative impact on the immune system each of these studies. When taking these results into account, it is evident that the effects of mental health on the synthesis of IgE may be a crucial area worth exploring further.

The first studies analyzed the relationship between asthma and psychological science concentrated primarily on the relationship between asthma, depression, anxiety and quality of life. These studies suggested that asthma was commonly accompanied by mental health difficulties; while all of the results in the literature were consistent with each other (Lavoie et al. 2005, Boran et al. 2008, Klinnert et al. 2008). However, it was also apparent that there was limited research that focused on the relationship between asthma and mental health from the aspect of the synthesis of IgE.

As a result, one of the main questions that has yet to be explored in more detail by the current literature is “Can serum IgE levels (which are affected by Th2 cells) impact the severity of asthma, due to presence of the stress factors mentioned in the literature?” The second and third questions that the current study aims to address is: “Are IgE

levels (mediated by Th2 cells and allergens) also affected by stress-induced mental disorders (same as Th2 cells),” and “Can its’ relationship with asthma become more statistically significant?”

The overall goal of the current study is to analyze the relationship between asthma (with serum IgE level) and the variables of mental health; while developing an additional perspective to support the treatment of individuals suffering from asthma. In this manner, negative effects of mental health problems on asthma prognosis can be easily controlled by using therapeutic interventions methods

Method

Sample

The ‘convenience sampling method’ was used in the data collection process of this study, where 148 participants were recruited. The sample group for this research comprised of pediatric patients ranging between the ages of 6-12 years old, who were admitted to the Pediatric Pulmonology and Pediatric Allergy Clinics of 4 university hospitals (126 participants) and 2 private hospitals (22 participants) in Istanbul Province and who also had a diagnosis of asthma. During the recruitment process, participants are selected randomly. The inclusion criteria of this study were being between 6-12 years of age, having a diagnosis of asthma or being treated for asthma (by a specialist) and having a measurement of total IgE in the past 2 weeks. Exclusion criteria were having a diagnosis of any psychiatric disease induced by drug use and having an allergic disease other than asthma.

In this study, seven participants were excluded in total. Three participants were younger than the age of 6, one participant was older than the age of 12 and three participants were diagnosed with one or more psychiatric diseases.

Procedure

For the sampling process, an application was made to the Koşuyolu Campus of Istanbul Medipol University Hospital and Approval of Ethics Committee for Multicenter Researches on 02.09.2015. Subsequent to this, an application was made to the Clinics of Pediatric Chest Diseases and Pediatric Allergy and these clinics also confirmed previously obtained Approval Ethics Committee for Multicenter Researches; to enable the participation of their patients. With regards to the data collection process, specialist physicians transferred the data of the patients in accordance with GINA criteria. In accordance with these criteria, the severity of asthma is evaluated based on the asthma control level, where the asthma control level is calculated by considering factors such as the grade of the symptoms, reduction in the values of pulmonary function tests, required medication dosage and daily activity limitations. Asthma level was rated in accordance to these parameters as “controlled”, “partially controlled” and “uncontrolled” asthma (GINA Report, 2016).

Subsequently, blood tests were requested by the specialist and participants gave blood on an empty stomach without any arrangement. Psychological evaluations were performed and statistical analysis process for the results were obtained from a total of 141 participants. Initially, parents were asked to sign the consent forms, followed by a sociodemographic form and somatic complaints subscale of Child Behavior Check List

Manual. In the psychological assessment process, children were instructed to apply scales. Statistical analysis was completed on SPSS (Version 16).

Measures

Revised Children's Manifest Anxiety Scale (RCMAS)

Developed by Reynolds and Richmond, "The Revised Children's Manifest Anxiety Scale, Second Edition" is used to evaluate the symptoms associated with anxiety which manifests itself without any underlying psychological problem in children aged between 6-19 years old (Reynolds et al. 1978). The researchers have noted that the first 10 items of this scale (from a total of 49 items) can be used as a short form to evaluate general anxiety and higher scores represents higher level of anxiety. The validity and reliability of the Turkish version was standardized by Çölümlü (2014), where the Cronbach's alpha (α) value was found to be 0.87. In this study, the short form referred to as MAS was used, whereby its' reliability coefficient was 0.87.

Pediatric Asthma Quality of Life Questionnaire (PAQLQ)

This scale was developed by Juniper et al. in attempt to measure physical, mental and social disorders associated with asthma in children aged between 7-17 years old (Juniper et al. 1996). This scale included 23 items and is comprised of three subscales which evaluate signs of asthma, limitation of activities and levels of emotional functionality. The Turkish version of the scale was standardized by Yüksel et al. (2009). A second validity and reliability test of the scale, aimed towards children aged between 6-17 years old, was performed by Aktan in a sample group of 211 participants (Aktan 2016). In this, the Cronbach's alpha value of the scale was found to be 0.83, when applied to children aged between 6-17 years old. Cronbach's alpha value within the current study was found to be 0.87.

Child Behavior Check List (CBCL/6-18)

The "Child Behavior Check List" (CBCL/6-18) includes eight subscales which evaluate anxiety-depression, social introversion/depression, somatic complaints (SC), breaking rules, offensive behaviors, social problems and attention deficits in the children aged between 6-18 years old. Items of the scale were prepared according to triple likert type response options and adapted to Turkish by Erol and Şimşek (2010). The Cronbach's alpha value of the subscale for somatic complaints from Child Behavior Check List (CBCL), which includes 8 items, was 0.76. The Cronbach alpha value was found to be 0.76 according to reliability assessment in our sample group.

Child Depression Inventory (CDI)

Prepared by Kovacs (1981) and based on Beck Depression Inventory, this scale can be applied from first year of primary education to the age of 17 and its original name is known as "Children Depression Inventory (CDI)". This scale comprised of 27 items uses triple likert response options and responses are scored as 0, 1 or 2; depending on the severity of depressive symptoms. The scores obtained from this scale range between 0-54 points, whereby the cutoff point is 19. Validity and reliability assessments of the Turkish version was standardized by Öy (1991) and reliability coefficient of this study was found 0.71.

Measurement of Serum IgE Levels and Assessment of Asthma Control Level

Blood samples from pediatric patients who were followed-up due to a diagnosis of asthma were analyzed by an ELISA (Enzyme-Linked Immuno Sorbent Assay) test in the immunology laboratory, where serum IgE levels were obtained over the 2 weeks prior. The asthma control level of each participant was determined by the specialist in accordance with GINA criteria, based on the levels of the control patients as follows; "controlled", "partially controlled" and "uncontrolled" asthma.

Statistical Analysis

The current study entailed 141 participants and statistical analysis was performed on SPSS (Version 16). The relationship between sociodemographic and clinical characteristics of participants was analyzed and an Independent samples T-Test was applied. Following this, Analysis of Variance (ANOVA) was conducted to determine if the psychological symptoms (anxiety, depression, somatic complaints and quality of life) and serum levels of IgE differences between asthma groups were statistically significant. Subsequently, Pearson Correlation Analysis was performed in order to analyze the correlational relationship between variables.

This study focused on the relationship between serum levels of IgE and asthma control levels of participants; whilst also analyzing the possible moderator effect of mental health conditions on this relationship. In this, asthma control level was the predicted variable, serum levels of IgE was the predictor variable and mental health conditions were the moderator variables. In order to analyze moderator effects of mental health variables, Hierarchical Regression analysis was conducted.

Results

Based on the GINA criteria, there were 91 participants with controlled asthma, 31 participants with partially controlled asthma and 19 participants with uncontrolled asthma; as shown in Table 1. In accordance to Table 1 35% of participants were female (n=50) and 64,5% were (n=91) male. Amongst male participants, 63,7% (n=58) were diagnosed with controlled asthma, 23,1% (n=21) were diagnosed with partially controlled asthma and 13,2% (n=12) were diagnosed with uncontrolled asthma. Amongst female participants, 66% (n=33) were diagnosed with controlled asthma, 20% (n=10) were diagnosed with partially controlled asthma and 14% (n=7) were diagnosed with uncontrolled asthma.

As shown in Table 1; 19.9% (n=28) of participants were 6 years old, 17.7% (n=25) were 7 years old, 20.6% (n=29) were 8 years old, 13.5% (n=19) were 9 years old, 10.6% (n=15) were 10 years old 8.5% (n=12) were 11 years old and 9.2% (n=13) were 12 years old. Based on number of siblings, 14.2% (n=20) of participants had no siblings, 41.8% (n=38) of them had 1 siblings, 26.4% (n=24) have 2 siblings, 12.1% (n=11) have three siblings, 3.3% (n=3) have 4 siblings and 2.2% of participants have 5 and more siblings. On the other hand, 48.2 (n=68) percent of participants were first-born children, 39% (n=55) were second-born, 9.9% (n=14) were third-born, 1.4% (n=2) were fourth-born and 1.4% of participants were fifth-born and/or younger within the family.

Table 1. Demographic characteristics of participants

Variable	Controlled Asthma	Partially Controlled Asthma	Uncontrolled Asthma	Total
Gender				
Girl	%66(n=33)	%20(n=10)	%14(n=7)	%35.5 (n=50)
Boy	%63.7(n=58)	%23.1(n=21)	%13.2(n=12)	%64.5 (n=91)
Age				
6	%22(n=20)	%12.9(n=4)	%21.1(n=4)	%19.9(n=28)
7	%17.6(n=16)	%19.4(n=6)	%15.8(n=3)	%17.7(n=25)
8	%24.2(n=22)	%19.4(n=6)	%5.3(n=1)	%20.06(n=29)
9	%12.1(n=11)	%12.9(n=4)	%21.1(n=4)	%13.5(n=19)
10	%8.8(n=8)	%9.7(n=3)	%21.1(n=4)	%10.6(n=15)
11	%9.9(n=9)	%9.7(n=3)	0	%8.5(n=12)
12	%5.5(n=5)	%16.1(n=5)	%15.8(n=3)	%9.2(n=13)

Clinical Characteristics

The means and standard deviations of each scale were evaluated. Initially, CDI points of participants were assessed in accordance to their gender, whereby an independent sample T-test was applied. Results indicated that, although males ($M=9.49$, $SD=5.15$) present more symptoms of depression than females ($M=8.50$, $SD=4.64$), there was no significant difference between male and female levels of depression ($F(1,138)=0.35$, $p>.05$). According to T-test results on RCMAS test performance of participants, although males ($M=3.97$, $SD=2.95$) presented with more symptoms of anxiety than females ($M=3.00$, $SD=2.40$) there was no a significant difference between these two groups ($F(1,139)=0.68$, $p>.05$). According to the T-test results on PAQLQ test performance of participants, although males ($M=88.19$, $SD=18.94$) present higher quality of life signs than females ($M=88.08$, $SD=18.52$) no significant difference was found between male and female quality of life levels ($F(1,139)=0.002$, $p>.05$). According to T-test results on somatic complaints subscale test performance of participants, although males ($M=431.21$, $SD=523.85$) present more signs of somatic complaints than females ($M=3.98$, $SD=3.19$), no significant difference was found between male and female levels of somatic complaints ($F(1,139)=0.549$, $p>.05$). According to T-test results on Serum Levels of IgE, although males ($M=431.21$, $SD=523.85$) had higher levels of Serum IgE than females ($M=354.93$, $SD=421.45$) no significant difference was noted between male and female serum levels of IgE ($F(1,139)=0.002$, $p>.05$).

Correlation between Asthma Levels, IgE and Mental Health Symptoms

In order to test homogeneity of variance, a Levene's test was used and results indicated that the sample groups displayed the same variances and average distance to the mean for the groups were the same ($p>.05$). Therefore, Pearson correlation analysis was applied as the second step of analysis (Table 2). Results indicated that there was a significant relationship between somatic complaints and quality of life ($r=-.268$, $p<.01$) and levels of depression ($r=.202$, $p<.05$). Moreover, there was a significant relationship between quality of life and symptoms of anxiety ($r=-.260$, $p<.01$) and depression ($r=-.412$, $p<.01$). Additionally, there was a significant relationship between levels of anxiety and depression ($r=.169$, $p<.05$) and serum levels of IgE ($r=.311$, $p<.01$) of participants. Following this, correlational analysis demonstrated that there was a significant relationship

onship between serum levels of IgE and asthma control levels of participants ($r=.245$, $p<.01$).

Table 2. The correlations between asthma levels, IgE and mental health conditions of participants

Scale	SC (n=141)	PAQLQ (n=141)	RCMAS (n=141)	CDI (n=140)	GINA (n=141)	IgE (n=141)
SC	1					
PAQLQ	-.268**	1				
RCMAS	.140	-.260**	1			
CDI	.202*	-.412**	.169*	1		
GINA	-.049	-.025	.121	-.074	1	
IgE	.066	-.034	.311**	-.102	.245**	1

SC: somatic complaints, PAQLQ: pediatric asthma quality of life questionnaire, RCMA: revised child manifest anxiety scale, CDI: child depression inventory, GINA: global initiative for asthma, IgE: Serum levels of immunoglobulin. * $p<.05$, ** $p<.01$.

Moderator Effect Analysis

According to literature, in order to conduct a mediator analysis, there must be a significant relationship between all variables (Baron and Kenny, 1986). However, there were any conditions in the literature for conducting a mediator analysis, it is believed that the correlational relationship between variables (Table 2) is sufficient for conducting a moderator analysis. Therefore, this step focused on the moderator effect of the mental health variables on the relationship between serum levels of IgE and asthma control levels of participants.

Table 3. Analysis of moderator effect of manifest anxiety using hierarchical regression

Model		B	B	p
1	Constant	.016		1.000
	IgE	.245	.245	.003
2	Constant	.016		1.000
	IgE	.229	.229	.009
	Manifest Anxiety	.050	.050	.563
3	Constant	.007		.932
	IgE	.236	.236	.008
	Manifest Anxiety	.124	.124	.471
	Manifest Anxiety x IgE	-.023	-.087	.619

Model 1 $R^2 = .060$, Model 2 $R^2 = .062$, Model 3 $R^2 = .064$, B= Burden of Regression, β = Beta Coefficient

The predicted variables of this analysis were asthma levels of the participants, while IgE levels consisted of the predictor variable. The moderator variables comprised of mental health variables such as levels of depression, anxiety, life quality and somatization. A relationship of moderator variable with predicted and predictor variables was not mandatory and the relationship between the two variables may show different effects such as elevation and reduction; therefore, correlative relationships shown in Table 2 may be found sufficient. The research results have shown that approximately 6% of total variance on asthma level was explained by IgE ($R^2=.06$, $p<.01$), however, predictive effect of manifested anxiety on asthma levels ($R^2\text{change}=.002$, $p>.05$) was not significant and explained only 0.2% of total variance.

The results obtained at this stage also include that determinative co-effect of IgE and manifested anxiety on asthma level was not significant and this effect could explain 0.2% of total variance on asthma level ($R^2\text{change}=.002$, $p>.05$). As a consequence, it

could be stated that moderator effect of manifested anxiety with respect to the relationship between IgE and asthma level is not significant ($B = -.50, p > .05$).

In Table 4, IgE, asthma level and CDI scores were determined respectively as the predictive variable, the predicted variable and the moderator variable. Results showed that IgE explained 7% of total variance on asthma level ($R^2 = .07, p < .01$). It was noted that predictive effect of depression explained only 0.3% of total variance ($R^2 \text{change} = .003, p > .05$) and formative effect shown by depression and IgE together had no impact on total variance ($R^2 \text{change} = .001, p > .05$). Consequently, it could be stated that depression shows a non-significant moderator effect on the relationship between IgE and asthma level ($B = -.25, p > .05$).

At the next stage in which predictive effect of somatic predisposition levels of the participants, with respect to the relationship between IgE and asthma level, the obtained data is shown in Table 5. The results indicate that IgE explains 6% of total variance on the asthma control level ($R^2 = .06, p < .003$) while 0.04% of total variance was explained by somatic predisposition ($R^2 \text{change} = .004, p > .05$). Analysis found that formative effect shown by somatic predisposition and IgE on asthma control level clarified 0.2% of total variance and that moderator effect somatic predisposition was not significant ($B = -.51, p > .05$).

Table 4. Analysis of moderator effect of depression using hierarchical regression

Model		B	β	p
1	Constant	.010		.907
	IgE	.266	.262	.002
2	Constant	.010		.908
	IgE	.261	.257	.002
	Depression	-.048	.048	.562
3	Constant	.007		.937
	IgE	.253	.249	.006
	Depression	.055	.055	.531
	Depression x IgE	-.028	.023	.802

. Model 1 $R^2 = .060$, Model 2 $R^2 = .062$, Model 3 $R^2 = .064$, B= Burden of Regression, β = Beta Coefficient

Table 5. Analysis of moderator effect of somatic complaints using hierarchical regression

Model		B	β	p
1	Constant	-.016		1.00
	IgE	.245	.245	.003
2	Constant	-.016		1.00
	IgE	.249	.249	.003
	Somatic Complaints	-.066	.066	.429
3	Constant	.003		.976
	IgE	.253	.253	.003
	Somatic Complaints	-.063	.063	.445
	Somatic Complaints x IgE	-.038	.043	.609

Model 1 $R^2 = .060$, Model 2 $R^2 = .064$, Model 3 $R^2 = .066$, B= Burden of Regression, β = Beta Coefficient

In the last stage of the research, predictive effect of quality of life with respect to the relationship between asthma level and IgE was examined, it was encountered according to the analysis results shown in Table 6. It was found that 6% of total variance was explained by IgE ($R^2 = .06, p < .004$) whereas predictive effect of quality of life was not significant ($R^2 \text{change} = .00, p > .05$). The formative effect of the interaction between life

quality and IgE on the predicted variable clarified 0.8% of total variance whereas moderator effect of life quality was also not significant ($B= 1.11$, $p>.05$).

Table 6. Analysis of moderator effect of quality of life using hierarchical regression

Model		B	β	p
1	Constant	-.016		1.0
	IgE	.245	.245	.003
2	Constant	-.016		1.00
	IgE	.244	.244	.004
	Quality of Life	-.017	-.017	.840
3	Constant	.005		.955
	IgE	.241	.241	.004
	Quality of Life	.011	.011	.903
	Quality of Life x IgE	.138	.096	.269

Model 1 $R^2 = .060$, Model 2 $R^2 = .060$, Model 3 $R^2 = .068$, B= Burden of Regression, β = Beta coefficient

In light of the aforementioned data, moderator effect of mental health variables with respect to the relationship between IgE level and severity of asthma in accordance with the initial purpose of the research and none of the mental health variables were found to have a moderator effect on the relationship between IgE level and severity of asthma. The results highlighted that there might be another way of analyzing the relationships between serum IgE, mental health variables and severity of asthma even though this was not one of the essential hypothesis of the research. Within this context, it is considered to centralize asthma control level of the participants in accordance with GINA criteria and it is planned to perform analyses to test whether the relationships between IgE and mental health as shown in Table 2 may vary depending on severity of asthma. The next section involves the results of this analysis.

Relationship between Serum Levels of IgE and Mental Health Variables Based on Asthma Control Levels

The probable relationship between the mental health variables and IgE was examined and the rate at which this relationship varied was shown based on asthma levels. The obtained data were shown in Table 7.

Table 7. Correlations between Serum IgE and mental health conditions in terms of asthma control levels

Scales	IgE Levels Controlled Asthma Group (n=91)	IgE Levels Partially Controlled Asthma Group(n=31)	IgE Levels Uncontrolled Asthma Group (n=19)	IgE Levels All Asthma Group (n=141)
PAQLQ	-.104	-.203	-.092	-.034
CDI	-.044	-.233	-.070	-.102
SOMA	.115	-.075	.297	.066
RCMAS	.002	-.011	.672*	.311*

SOMA: somatization subscale of child behavior check list, PAQLQ: pediatric asthma quality of life questionnaire, RCMAS: revised children's manifest anxiety scale, CDI : child depression inventory, GINA: level of asthma, IgE: serum level of Immunoglobulin E, * $p<.002$.

Following this, the scores of the participants obtained in the Pediatric Asthma Quality of Life Questionnaire were taken into account and were comparatively analyzed by evaluating each asthma group separately and all the asthma groups simultaneously to establish how these scores varied. As shown in Table I, the correlative relationship between the quality of life levels and IgE levels of the participants were non-significant

when all the asthma groups were analyzed together ($r=-.034$, $p>.05$) while the same correlative relationships were also found to be non-significant in the controlled ($r=-.104$, $p>.05$), partially controlled ($r=-.203$, $p>.05$) and uncontrolled asthma groups ($r=-.092$, $p>.05$).

Subsequently, the relationship of the scores obtained in CDI with IgE were analyzed. The relationship between the IgE levels and depressive scores of the participants were found to be non-significant ($r=-.102$, $p>.05$) when the analysis involved all the groups together while this relationship remained non-significant in the analyses of the controlled ($r=-.044$, $p>.05$), partially controlled ($r=-.233$, $p>.05$) and uncontrolled asthma group ($r=-.070$, $p>.05$) separately.

Correlative relationships between the scores of the participants obtained from the subscale of somatic complaints and serum IgE levels were analyzed, these relationships were found to be non-significant, which involved all the asthma groups together ($r=.066$, $p>.05$). This relationship remained non-significant when the controlled asthma ($r=.115$, $p>.05$), partially controlled asthma ($r=-.075$, $p>.05$) and uncontrolled asthma group ($r=.297$, $p>.05$) were analyzed separately.

During the final stage of the analysis, the correlative relationships between the scores of the participants gained from the manifest anxiety scale and serum IgE levels were surveyed, stages of the correlation analyses were performed by initially considering all the asthma groups together, and then considering them separately as subgroups. According to the results, correlative relationship between the manifest anxiety scores and IgE levels of the participants were found to be significant ($r=.311$, $p<.01$) when all the groups were analyzed together. However, this relationship was found to be non-significant, based on the controlled asthma group ($r=.002$, $p>.05$) and partially asthma groups ($r=-.011$, $p>.05$) when the subgroups were analyzed separately. With respect to the correlative relationship between manifest anxiety scale scores and serum IgE levels of the uncontrolled asthma group, it was observed that this relationship remained statistically significant at a moderate level and highly correlated ($r=.672$, $p<.002$); beside dramatical elevation of the correlation coefficient..

Discussion

The purpose of this study was to examine the relationship between the control level of asthma, mental health problems and Serum levels of IgE. According to the analysis presented in the literature, the researchers investigated significant relationship between asthma and mental health (Çevik 2011, Kartaloglu 2011, Goodwin et al. 2013) asthma and serum levels of IgE as an indicator of immune system in asthma (Lambrecht et al. 2015, Borish 2016) and immune system and mental health separately (Murali et al. 2007, Leonard 2010), while no other study seems to have investigated these relationships together. Therefore, the current study aimed to clarify the nature of these relationships, by aiming to identify the probable role of serum IgE; which is accepted as a more comprehensive indicator of the immune system.

The moderator model of the current study was conducted in accordance to literature review which demonstrated significant relationships between immune system, mental health and chronic diseases specifically; HIV, cancer amongst others (Ironson et al. 2005; Crepez et al. 2008; Barnett, 2008). Moreover, this work also aimed to shed light on an understudied area of health related to asthma as a chronic disease.

The first step of the current work, which focused on the correlational relationship between asthma control level, Serum levels of IgE, anxiety, depression, somatic complaints and quality of life in asthma; results indicated that there was a significant relationship between somatic complaints with quality of life and depression, a significant relationship between quality of life with manifested anxiety and depression, a significant relationship between manifest anxiety with depression and serum levels of IgE and a significant relationship between asthma control levels and serum levels of IgE.

These results demonstrated that higher somatic complaints may be related to lower levels of quality of life and this relationship may also have negative effects on levels of depression. On the other hand, according to results it is clear that a lower quality of life may also affect depression and anxiety levels of the participants and the levels of anxiety and depression are getting higher. One of the crucial results of this study is the significant relationships between serum levels of IgE, manifested anxiety and asthma control levels of participants. According to this result, higher anxiety levels predict higher levels of serum IgE and higher levels of serum IgE has negative effects on asthma control levels of participants. When taking into account negative effect of anxiety on asthma, it is clear that psychotherapy interventions may have positive effects on the treatment process of asthma.

According to literature, there are a considerable number of studies that partially support the findings of the current study. However, although limited research focused on the relationship between somatic complaints, quality of life and depression in asthma, studies conducted with healthy samples supported our findings. More specifically, Kounou et al. (2017) focused on the relationships between levels of post-traumatic stress, somatization and quality of life among immigrants, whereby their findings showed a significantly negative correlation between quality of life and somatization. Moreover, a great deal of work that focused on the relationship between somatization and depression suggested that there are significantly positive correlations between the two variables (Katon et al. 1928, Kapfhammer 2006).

In a previous study, Çoban (2018) focused on the relationship between quality of life and anxiety among asthma groups and his findings were compatible with our study. According to results there is a significantly negative correlation between quality of life and anxiety levels of asthma patients. Moreover, their levels of depression also negatively correlated with their quality of life. Additionally, several studies focusing on the relationship between depression and anxiety demonstrated similar results with findings of the current study. Specifically; Malone et al. (2018) suggested that there are positively significant correlations between depression, anxiety and well-being.

The results of studies which focused on the relationship between manifested anxiety and Serum IgE related allergic reactions also partially supported current findings. Specifically, Gregory et al. (2009) focused on the relationship between anxiety and allergens. Results indicated that self-report allergic symptoms highly correlated with anxiety; however, when allergic symptoms were assessed objectively, results indicated non-significant correlations.

The literature focusing on the relationship between asthma control level and serum IgE demonstrated similar findings with our study (Rotsides et al. 2010, Lama et al. 2013, Tanaka et al. 2014). Specifically, Lama et al. (2013) claimed that there was a significant relationship between asthma controls and serum IgE levels of participants.

Moreover, it was suggested that higher levels of serum IgE predicts lower levels of asthma control.

When taking the findings between mental health, asthma and serum IgE into account, the first hypothesis of current work focused on the moderator effect of mental health variables on the relationship between asthma and serum levels of IgE. In this model, the predictor variable was serum levels of IgE, predicted variable was asthma control level and moderator variable is mental health. Linear hierarchical regression analysis was used for moderator effect analysis of the mental health variables and results of the analysis demonstrated that moderator effect of respectively depression, manifest anxiety, quality of life and somatic complaint scores on the relationship between asthma control level and IgE was statistically non-significant.

When reviewing the literature overall; it is evident that many studies have investigated asthma, mental health immunity level in the clinical picture of asthma separately; while limited research explored this relationship by developing a moderator model. However, some of the previous studies demonstrated similar findings with the current one. Specifically, in their previous work Lama et al. (2015) found that there was a strong correlation between asthma control level and serum IgE. Moreover, work by Rotsides et al. (2010) with a New York sample also demonstrated similar findings. It was stated that there was a significant relationship between asthma control and serum levels of IgE among children. There is also a considerable amount of literature which focused on the relationship between asthma and mental health. According to the findings of these studies the most significant correlations between asthma and mental health problems indicated that anxiety related difficulties and these findings also support the results of the current study (Demirci 2008, Di Marco et al. 2010, Lavoie et al. 2005).

There was also a considerable number of studies which aimed to clarify the pathophysiology of asthma. Particularly, the studies of Murali et al. (2007) who have reported that Th2 count was reduced by the effect of stress and this condition caused weakening of the immune system and Saggini et al. (2011) who have reported synthesis of IgE is affected by Th2 cells were quite remarkable. These results make the conclusions more important that serum IgE level synthesized by Th2 cells may be affected by stress-induced mental health variables and that the relationship between IgE and mental health variables; as well as Th2 should be evaluated. Therefore, it's clear that future research should also focus on the role of Th1 and Th2 cells in asthma and their relationship with synthesis of IgE in order to explore the nature of asthma more in detail.

Since the current study was unique in its approach, advanced analyses to examine the relationship of IgE levels with mental health variables and also severity of asthma even though this issue was not one of the essential hypotheses of the study since study data should be analyzed comprehensively and all the obtained results should be reported. In this context, it was concluded that the asthma control levels of the participants should be centralized in accordance with GINA criteria and it was concentrated whether non-significant relationships between Serum IgE and mental health show any elements of variation.

According to the results of the analysis, a non-significant relationship of serum IgE level with depression, quality of life and somatization when all the asthma groups were evaluated together remained statistically non-significant; including after analysis of the

asthma groups separately. In other words, the relationship of serum IgE level with depression, quality of life and somatization did not vary depending upon asthma control level. However, analysis of the relationship between the scores of the anxiety scale showed a moderate level correlative relationship, when the analysis involved the asthma groups together whereas this relationship became non-significant only when controlled and partially controlled asthma groups were included in the analysis. In the analysis of the uncontrolled asthma group it was observed that correlation coefficient of the significant relationship increased dramatically compared with its previous value, while significance level of the relationship also increased.

In the light of the aforementioned data, the most noticeable result was the dramatic elevation of the anxiety level of the participants; especially in the uncontrolled asthma group. In other words, these results indicate that lower level of asthma control predicts higher levels of anxiety; therefore it is clear that psychotherapy interventions may have crucial effect on asthma treatment. In the review of past literature which can be associated with this result, it is possible to detect several studies with similar results. For instance, Thoren and Petermann (2000) have presented similar data and stated that the perception and interpretation style of the children with higher levels of anxiety included more intense disaster scenarios than the children without anxiety; while number of the seizures of the children with higher anxiety level increased more frequently and these children had stronger symptoms compared with other children (Thoren and Petermann 2000, Kotrotsiou et al. 2011).

Although the findings of this study showed a non-significant moderator effect, the nature of the relationship between variables may help to conduct a different hypothesis. Specifically, if the results of the study conducted by Saggini et al. (2011) which suggest that synthesis of IgE is affected by Th2 cells are combined with the results of the trials conducted by Murali et al. (2006) which presented significant correlations between Th2 count and stress, it could be concluded that the probable role of Th2 should be investigated in conjunction with the role of serum IgE level.

Studies which focused on the relationship between asthma, mental health and immune system have some limitations, as does the current study. For instance, the current work used a convenience sampling method in the participant recruitment process. As such, this sampling method has several limitations related to its reliability. Additional limitations entail the fact that the participants of the current study could not be equally placed in to asthma control groups, their socio demographic characteristics could not be equally split into groups, research sample of current work was limited and it was difficult to access uncontrolled asthma group. When taking these limitations into account, it can be concluded that these may contribute to non-significant findings.

The more notable outcomes of the current study were strength of the correlative relationship between the levels of anxiety and IgE levels of the participants, and the fact that asthma level is an important predictive impact in terms of manifest anxiety level although uncontrolled asthma group included 19 participants.

Finally, in the light of all these results, it can be concluded that construction of the studies in the future should consider all these features when attempting to clarify the relationship between asthma, mental health and immune system more comprehensively. Consequently, asthma can be controlled and life quality level of the asthma patients can be increased, as well as reduction in the treatment costs by adding novel treat-

ment models of asthma as a chronic disease.

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