Exploring Role of Some Physiologic Biomarkers and Serum Parameters in Early Detection and Progression of Asthma in the Iraqi Population.

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Abstract

Asthma is a common chronic lung disease in which the airways (bronchi) become inflamed and are abnormally sensitive to certain triggers. Asthma can affect people of all races and ages, and although there is no known cure, there are many ways to control it. The symptoms of asthma include coughing, shortness of breath, wheezing, and chest tightness. This study was carried out in Al-Sadr Teaching Hospital/ Allergy and Asthma Center and Al-Hakim Hospital/ Chest and Respiratory Diseases Center in Al-Najaf province -Iraq and laboratory of molecular biology in the Department of Biology / Faculty of Science – University of Kufa. The study population was included 70 Asthma and 20 healthy subjects. The estimated incidence of Asthma in the age group 33-51 years with a percentage of 55.71% recorded a significant increase (P<0.05) compared to the rest of the age groups, followed by the age group 15-32 years with a percentage of 24.29% and 52- 70 years with a percentage of 20%. The levels of erythrocyte sedimentation rate (ESR) in patients and the healthy group, where the results of the study showed a significant increase (P<0.05) ESR of the patients (22.77±1.98 mm/hr) compared with the healthy group (14.20±2.86 mm/hr). The cortisol variable recorded a significant decrease (P<0.05) in the patients (6.51±0.62 g/dL) compared with the healthy group (11.82±0.81 g/dL). The results recorded a significant increase (P<0.05) for non-smokers by 84.29% compared with smokers who scored 15.71%. The reason for the prevalence of asthma among smokers is that smoke irritates the airways, thus making them swollen, narrow, and filled with sticky mucus - the same things that happen during an asthma attack, this is why smoking can cause asthma flare-ups (or so-called "attacks"). Oftentimes, they may also be more severe and difficult to control, even with treatment with medication. And the results of the current study indicated that there is a relationship between frequency of blood group (A) and (B) with asthma in patients compared with the group of controls

Keywords: Asthma, cortisol, erythrocyte sedimentation rate, ABO blood groups.

1. Introduction

Asthma is a chronic illness of the broncho airways that commonly manifests as wide whistled sounds (wheezing) when breath in people with the condition [1]. The term "asthma" is derived from a Greek word that means "breathing heavily" or "struggling to breathe," and it was first described by Pythagoras, an Ancient Greek clinician [2]. It has also been demonstrated that interplay of heredity and environmental factors caused asthma, and that some characteristics of asthma were substantially influenced by a genetic pattern but not by Mandli's pattern [3-5]. As a result of increasing air pollution exposure, global warming, changes in immunological response, urbanization, and lifestyle changes [6, 7], Rackeman categorized asthma as "extrinsic" asthma (onset before the age of 30 years) and "intrinsic" asthma (beginning after the age of 40 years) in 1947 [8]. The officially European Association of Allergies and Clinical Immunol (EAACI) policy statement subsequently updated this nomenclature in 2001. "Extrinsic" and "intrinsic" asthma have been superseded by "allergic" and "non-allergic" asthma, correspondingly [9]. Miranda et al. [10] coined the terms "slightly earlier asthma" (EOA) and "lately-onset asthma" (LOA) to distinguish asthma based on the age of the onset [10]. The Global Initiative for Asthma (GINA) strategy for 2020 identifies LOA as being one of the disease phenotypes of asthma in which clients, particularly women, show with asthma for the first single time in adult hood, are non-allergic, and usually requires an increasing dosage of systemic corticosteroids (ICS), or are comparatively highly resistant to corticosteroid therapies [11].

2. Aim study

1- Measuring the physiological parameters of cortisol and erythrocyte sedimentation rate in asthmatic patients and knowing their relationship to asthma.
2- Attempting to find the relationship between ABO blood groups and asthma cases.

3. Methods

Samples collection and bacterial isolation

3.1 Sampling of Cases

a) The group consists of 70 patients. They were admitted to Allergy and Asthma Centers. All the patients selected for the present study were having asthma.
b) The group consists of 20 healthy individuals; all were without any inflammatory disorders or clinical manifestation of any disease.

3.2 Blood Samples

Tests were performed on 5 ml of venous blood, which was

doi.org/10.31838/hiv22.02.47 Received: 19.01.22, Revised: 19.04.22, Accepted: 07.08.22

collected from asthma patients and the control group.

1. 2ml was collected in gel tubes centrifuged at 5000 rpm for 5 minutes; 0.5 ml serum was used for the cortisol test.
2. 1 ml was collected in tubes with anticoagulant EDTA: used for blood group.
3. 2 ml was collected in tubes with sodium citrate used for ESR tests

3.3 Physiological Tests

3.3.1 Cortisol

Cortisol levels were measured using an AIA-360®analyzer (TOSOH Bioscience GmbH, Griesheim, Germany) after blood tests were centrifuged immediately to prepare serum [12]. This analyzer uses a competing fluorescent immunochemical format that is carried out entirely within small, single-use test cups containing all necessary chemicals. The substance in the samples compete with the enzyme-labeled hormones and is exposed to a fluorogenic substrate, phosphate 4-methylumbelliferyl. The amount of enzyme-labeled hormonal that connects to the bead is relative to the quantity of hormone in the sample test. Calibration, daily inspections, and maintenance were carried out in line with the System Operator's Manual. Previously, accurate cortisol test data, including analytical recoveries and diluting tests, had been analyzed but were accessible in the manufacturer's technology bulletin. This test produces an initial result in 20 minutes, with subsequent data received every minutes then after. Serum sample (150L) was placed in testing tubes, and hormonal levels were measured using the immunoassays described above. Cortisol levels were lower (and higher) than the published levels of 2.0 (2000.0) pg/mL in cortisol tests

3.3.2 The erythrocyte sedimentation rate

The erythrocyte deposition rate (ESR) is the rate at which erythrocyte cells deposit. ESR is still commonly used to assess acute-phase response screening. In addition, monitoring test for infection, autoimmune and malignant diseases. The examination has been done ESR by ESR Rack PP/ ESR:

The venous blood was collected according to standard requirements in a 9x120 mm ESR vacuum tube, containing sodium citrate, The tube was immediately inverted at 180 degrees 6-8 times for mixing thorough, to avoid hemolysis, clotting, or bubble, At the room temperature of around 20°C, the ESR tube containing the blood sample placed vertically onto the rack, notes the starting time and relevant numbers. Was kept the rack still for 30 minutes and then read the millimeter of erythrocyte sedimentation, Detailed reading method: it was kept stable for 30 min, was align the plasma concave in ESR tubes to the zero scares of the ESR fast rack. Then, the data was read by aligning the upper surface of the erythrocyte to the scale on the rack.

3.3.3 ABO Blood group by Slide or tile method

Relax the hand to increase blood flow to the fingertips. Use spirit or 70% alcohol to clean the fingertip to be pierced (Typically, the ring or middle finger).Using the sterile lancet, puncture the fingertip and insert 1 drop of blood in each cavity. Fill each cavity with one drop of antiserum. Using a new mixing stick, combine each blood drop with the antiserum. Within 30 seconds, look for agglutination in the form of tiny red granules [13].

3.3.4 Body mass index

The BMI value included the ratio of weight and height squared (in kilogram and respectively)
for each patient, which was calculated according to the following universal form BMI=Wt (kg)/ Ht (m). The range of BMI for an adult was as follows: 18.5-24.9 kg/ considered as healthy or normal BMI, 25-29.9 kg/m was considered as overweight, and then 30 kg/m was considered as obese.

3.3.5 Statistical analysis

The spss-V24 program was used to analyze the data by means of the Independent Samples T-test to find statistically value differences.

4. Results and Discussion

Asthma is a complex disease consequence of the interaction of intrinsic and extrinsic factors; the current study focused on the possible relation between cortisol and ESR. We found significant Diagnostics differences in some demographical variables, like sex, age, and the BMI

4.1.1 Gender

The clinical assessment revealed that the frequency of distribution of patients according to gender were 32 (44.29%) females and 38 (55.71%) males (Figure 4.1). The differences in gender were statistically not significant (P< 0.05)

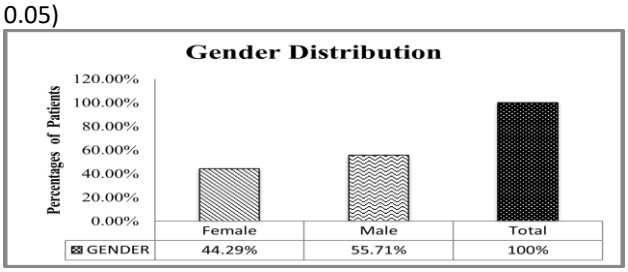

Figure 4.1: The frequency of distribution of patients according to gender.

The findings of our study agreed with those of Wisamkadhum [14] at the Teaching Hospital in Baghdad, who found no significant difference between women and men in terms of asthma, with the men's category recording 17 samples with a rate of 45.9 percent and the female category recording 20 samples with a rate of 54.1 percent. While Al-Smaism et al. [15] at the Allergy and Asthma Clinic in Hilla City found no significant differences here between the men category 21 asthma patients and the female category 20 asthma patients. The findings contrasted from Li et al. [16] in that there was a substantial rise in 60.4 percent of females with asthma compared to 39.6 percent of males. The findings contrasted from Li et al. [16] in that there was a substantial rise in 60.4 percent of females both with asthma compared to 39.6 percent of males. While the researcher [17] carefully explained that there were substantial disparities between males and females among patients with asthma, the research stage that there is a

considerable rise in women because hormonal status may promote the difference between the sexes since it seems that ovarian hormones rise, and it appears which the hormone Testosterone lowers bronchial inflammation through unknown processes; However, estrogen levels are likely to fluctuate, as is the impact of oral contraceptives. Indeed, estrogen receptors (ERs) were mostly present in the lung, including smooth muscle cells, with no difference between males and females, but the comparative mutual involvement of ER and ER in terms of bronchoconstriction was determined by the microenvironment and hormonal level. Eosinophilia, IgE secretion, and airways hyperactivity were decreased by dilatation and oophorectomy.

4.1.2 Age

The results of the study showed, as in (Figure 4.2). where the age group 33-51 years recorded a significant increase (P<0.05) by 55.71% compared to the rest of the age groups, followed by the age group 15-32 years with a percentage 24.29% and 52- 70 years with a percentage 20%.

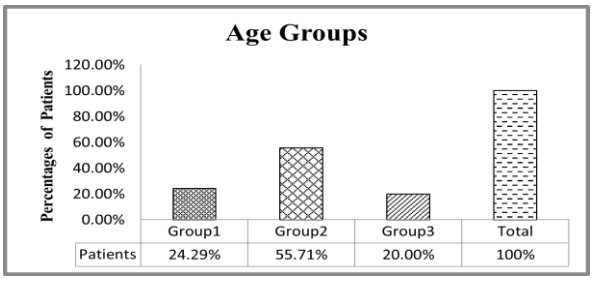

Figure 4.1: Age distribution of patients presented with asthma. (Group1: 15-32, Group2: 33-51, Group3: 52-70).

The findings of this study corresponded with those of Abed [18] in Baghdad hospitals, which found that the majority of asthmatic patients (62 percent) are men with ages ranging from 30-39 years and that the age group to asthma had a poorer level of physical well-being than the younger ages.

While a research of Salman et al. [19] at Baghdad teaching hospital and Al-Yarmook teaching hospital found that the age group of asthma patients between 40-49 years made up the biggest percentage (46 percent), followed by the age group 30-39 years, and the majority of the study samples were (38 percent) [20]. By documenting those 68 asthmatic patients who had been diagnosed with asthma, the findings of our study agreed throughout Dour City in Salahaddin province. There were 38 male patients and 30 female patients. Patients range in age from 20 to 75 years old, with females being 31 to 40 years old and males being 41 to 50 years old. The findings of this study were consistent with the findings of another study [21] on the epidemiological data of the asthma prevalence in the Mideast (adults in the Kingdom of Saudi Arabia), which found a significant rise in patients with asthma in the age group 35-55 years, reaching 42.1 percent, followed by the group 55-70 years, by 25.8 percent There were many interpretations among researchers about the greater prevalence of asthma among the age group between (33-51 years), the youth group is higher than in the other groups (children and the elderly), because some of them reported that young people born prematurely (23-27 weeks gestation) were 2.4 times more likely to have it than those who had given birth after a lengthy late full-term pregnant women (28-32 or 33-36 weeks gestation), and the medicines used played a significant role [22].

4.1.3 Variable Erythrocyte Sedimentation Rate in patients and healthy group

The table shows the levels of erythrocyte sedimentation rate (ESR) and cortisol in patients and the healthy group, where the results of the study showed a significant increase (P<0.05) ESR of the patients (22.77±1.98 mm/hr.) compared with the healthy group (14.20±2.86 mm/hr.).

Table (4.2): Levels of Erythrocyte Sedimentation Rate in patients and healthy group

Groups Parameters	Patient 70	Control 20	p-value
	Mean±S.E		
ESR (mm/hr.)	22.77±1.98	14.20±2.86	0.036*
* Significant difference at P≤0.05.			

The findings concurred with Canöz et al. [23] in his investigation of the relationship of asthma and obese with inflammatory markers like ESR, CRP, and fibronectin levels, where ESR rates were greater in asthma patients than in the control group, attributed this to the link between high ESR and obesity. In addition, the study [24] saw a considerable rise in ESR levels in 40 asthmatic patients, with the patient population recording 19.875.82 mm/hr. Asthma is a possible risk factors for iron - deficiency anemia and low haemoglobin, red blood cells, ferri, an inflammatory reaction that relates asthma to the release of hepcidin, the "iron-regulating hormone," which inhibits iron intake and use of stored iron, 9.9 2.48 mm/hr. The results concurred with Hailemaryam et al. [25] showing a substantial rise in ESR values in the asthma group 29.68 21.05 mm / h compared to the healthy group 5.98 5.02 mm / h. Increased erythrocyte sedimentation rate (ESR) in asthma patients may be due to inflammatory mediators IL1 and mast cell-mediated TNF-, basophils, and macrophages Because these mediators drive the liver to create acute-phase proteins such as fibrinogen proteins, the positive charge, and buildup of red blood cells. it consists of intercellular increases in ESR in asthma patients.

4.1.4 Variable Cortisol in patients and healthy group

The table shows the levels of the cortisol variable recorded a significant decrease (P<0.05) in the patients (6.51±0.62 g/dL) compared with the healthy group (11.82±0.81 g/dL)

Table (4.1): Levels of cortisol in patients and healthy group, as for the significant decrease in cortisol levels in patients compared to the healthy group

Groups Parameters	Patient 70	Control 20	p-value
	Mean±S.E		
Cortisol (g/dL.)	6.51±0.62	11.82±0.81	0.0001*
* Significant difference at P≤0.05.			

The researcher [26] found this significant reduction in his study of 206 asthma patients who had low levels of cortisol compared to healthy control group, that poorly controlled asthma can lead to chronic stress and lower cortisol levels in adult asthmatic patients, that disease is the leading cause can lead to comment stress, which is

directly connected to patients' preconceptions of their asthma attacks, and that stress lowers levels of cortisol naturally produced by the hypothalamus. For instance, the next time they are exposed to a stimulus, they may struggle to control the amount and duration of a airway inflammation. Another long-term consequence might be reduced sensitivity to glucocorticoid medications, which are essential for efficient therapeutic control of asthma symptoms. This resistance to glucocorticoids may help to explain the dilemma that stress is not useful for asthma if it rises hypothalamic-pituitary-adrenal (HPA) axis activity. These findings suggest that when psychological stress first starts, there is an initial activation of the Hypothalamic - pituitary, resulting in higher ACTH and cortisol concentrations, However, as time passes, this activity decreases and cortisol secretion recovers to normal levels. If this mechanism results in a lack of GR signaling in lymphoid tissues, it may have some of the same effects for asthma sufferers as stress-related glucocorticoid sensitivity [27].

4.1.5 Body mass index (BMI)

The results of the current study on body weight among patients with asthma, according to (Figure 4.5) indicated that there were no significant (P>0.05) differences between weight categories of asthmatic patients.

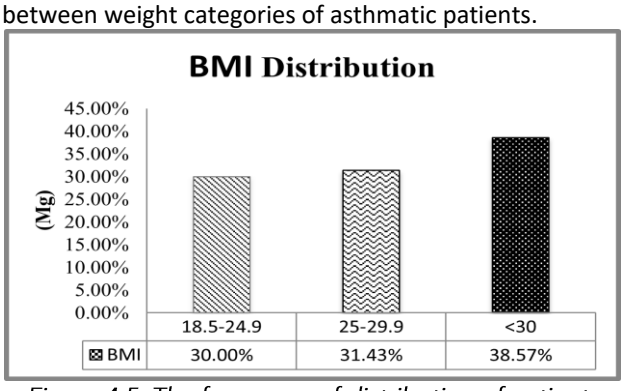

Figure 4.5: The frequency of distribution of patients according to BMI

A study [18] conducted in teaching hospitals in Baghdad governorate on the quality of life of asthmatic patients revealed found there were no significant differences in asthmatic weight and that there was no association between the physiological and weight axis of asthma patients and the other factors (such as age, gender, and level social), The pathogenic symptoms in obese individuals were twice as severe as in underweight people, according to the study. Patients with a BMI of 30 or higher had a higher risk of developing asthma than those with a lower BMI, Asthma affects 7% of adults with a BMI in the normal range, but 11% of adults with an obese BMI. Excess weight around the chest and abdomen can constrict the lung tissue and make breathing more difficult. Fat tissue also produces inflammatory compounds that can impair lung function and lead to asthma.

While the findings agreed with those of Taylor et al. [28], who looked at the relationship of patients' body weight to some variables in 406 sick people, there were no significant differences among body weights of asthma patients; it is unlikely that it would lead to a differential bias in the BMI classifications index, However, a link was discovered between obesity and a raise in the severity of asthma in adults, as well as an increased risk of developing asthma in obese patients. Asthma and obesity interact and are linked to poor asthma health, more frequent exacerbations, and poor quality of life, indicating that obesity contributes to an increased burden of disease for asthma.

4.1.6: Relationship between asthma with smokers and non-smokers

The results of our study indicated according to Fig 4-6, which indicates the relationship of asthma with smokers and non-smokers, the results recorded a significant increase (P<0.05) for non-smokers by 84.29% compared with smokers who scored 15.71%.

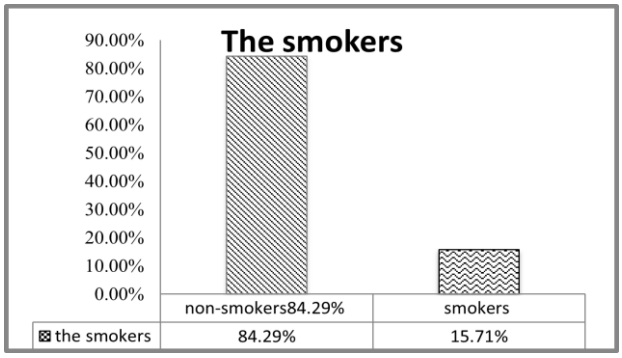

Figure 4.6: Relationship between asthma with smokers and non-smokers

The findings of our study corresponded with those of Muhammed et al. [29], who found a low proportion of smokers with asthma in the outpatient clinic of Baghdad Teaching Hospital, with a rate of 21.7 percent for 49 patients who have been passive smoker compared to 175 samples of non-smokers. During the researcher's [30] There was a considerable increase in the frequency of nonsmokers with asthma (55 samples) compared to 40 samples with asthma patients, explaining why corticosteroid therapy was ineffective in smokers with chronic asthma. When compared to nonsmokers with asthma, asthmatics in the current research had a considerably poorer therapeutic response.

The study agreed with [31] in his study of relationship of asthmatic patients with gender and smoking, in which the study recorded 858 samples for nonsmokers with asthma comparison to 292 samples for smoking of the female gender, whilst also males with asthma recorded 817 samples for nonsmokers compared to 205 samples, and they did not agree. The researcher records substantial variations in the prevalence of asthma between the sexes males 1741 samples and females 1637, various studies that found that current smokers had low levels of (FENO) Fractional exhaled nitric oxide, numerous plausible theories explaining this result, Such as suggestions that smoke may lead to a reduction in FENO metabolism or that smoking may cause a decrease in the activity of oxidant synthases in the airway.

4.7 The family history of patients with asthma

The results of the study, according to Figure 4-6, which shows the family history of asthmatics, indicated that there were no significant differences (P>0.05) between the presence and absence of a history of asthma.

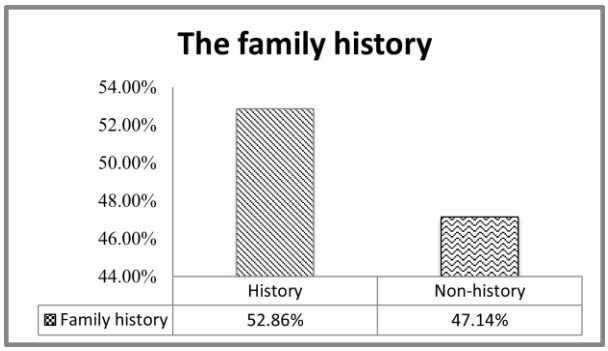

Figure 4.7: The family history of patients with asthma

In his study on the history of asthma, the researcher [28] noted that initial onset of asthma related symptoms to a trigger (actual or prospective immune response) occurs after just a latent exposure period, which can vary from weeks to years, as opposed to the onset of asthma caused by irritation, which typically begins within 24 hours of heavy exposure to irritants. Once the allergen is present, exposure-related asthma symptoms can range from immediate (i.e., within minutes of increased allergen exposure) to delayed (usually 4-6 hours after exposure, more commonly as an isolated response when the allergen is a potentially relevant factor). On the other hand, it could be a dual asthmatic reaction (responding followed by delayed response), and while history is an important part of making a diagnosis, the recent study found that incorrect prediction from history alone in 26 percent of those with a positive asthma response, confirming the need for more evaluation of those with a positive asthma response.

According to Liu et al. [32], family history of asthma is an essential risk factor for asthma, that relatives evaluations can help to identify people at high risk of respiratory disorders, and that more research is required to assess how experts can Health care Using family background information in early diagnosis and intervention of asthma [32].

4:8 Frequency distribution relationship between asthmatic patients and ABO

The results of the current study indicated that there is a relationship between the frequency of blood group (A) and (B) with asthma in patients compared with the group of controls

Table (4.3): Frequency distribution relationship between asthmatic patients and ABO

ABO Blood group	Controls (%)	Asthma patients (%)
A	10 (50%)	33 (47.14%)
B	5 (25%)	20 (28.57%)
AB	3 (15%)	11 (15.71%)
O	2 (10%)	6 (8.57%)
Total	20	70

This study's findings are comparable to those of Bijanzadeh et al. [33], who evaluated 239 German patients with diseases (atopic dermatitis, hay fever, allergic rhinitis, bronchiolitis, acute urticaria) and found probably greater antigens of blood type (A and B) in the control group [34]. Similarly, he researched [34]. Coal miners (228 patients) were found to have asthma, and lung function was shown to be reduced in blood type A and, to a lesser extent, blood group B. However, Khetsuriani et al. [35], [36] found that asthma induced by persistent pneumonia is more frequent in group B.

The current study's findings contrasted with those of Bijanzadeh et al. [33], who found that blood type (O) is more prevalent among asthmatic patients, followed by blood types (B, A, and AB), with a non-significant difference between patients and healthy controls. According to Koers et al. [37], blood group (B) is more susceptible to pollen than some other blood groups. However, no statistically significant difference between patients and controls was found in that investigation. In another research, blood type O/excreted (Se/Se) and O/Le (ab-) secretions were linked to childhood asthma and may be one of the prominent variables in environmental allergens in Taiwanese children [37].

5. Conclusion

The current study indicates that males are more likely to suffer from asthma compared to women, and female ovarian hormones, including testosterone, play a role in reducing bronchial infections by unclear mechanisms. The age group (33-51 years) had the highest rates of infection with the rest of the age groups. Asthma poses a challenge for young patients with chronic diseases, smokers, and obese patients. The elevated levels of the erythrocyte sedimentation rate (ESR) are a good flag for allergic or inflammatory conditions. In addition, the decrease in cortisol in asthma patients is related to the relationship of cortisol levels to the receptors of the pituitary gland axis. In addition, the ABO group (A) gave the highest percentage compared to the rest of the groups.

6. Acknowledgments

This research is accomplished in Kufa University/ Faculty of Education for Girls / Department of Biology

References

1. Global Initiative for Asthma. Global strategies for asthma management and prevention [Internet]. 2011 [cited December 13, 2013]. Available from: http://www.qu.edu.qa/pharmacy/professional_development/documents/GINA_Report_2011-1.pdf

2. Diamant Z, Diderik Boot J, Christian Virchow J. Summing up 100 years of asthma. Respiratory Medicine. 2007;101(3):378-88. https://doi.org/10.1016/j.rmed.2006.12.004

3. Baldini M, Carla Lohman I, Halonen M, Erickson RP, Holt PG, Martinez FD. A Polymorphism* in the 5′ flanking region of the CD14 gene is associated with circulating soluble CD14 levels and with total serum immunoglobulin E. American journal of respiratory cell and molecular biology. 1999;20(5):976-83. https://doi.org/10.1165/ajrcmb.20.5.3494

4. Pedersen SE, Hurd SS, Lemanske Jr RF, Becker A, Zar HJ, Sly PD, Soto-Quiroz M, Wong G, Bateman ED. Global strategy for the diagnosis and management of asthma in children 5 years and younger. Pediatric pulmonology. 2011;46(1):1-17.

https://doi.org/10.1002/ppul.21321
5. Rennie DC, Karunanayake CP, Chen Y, Nakagawa K, Pahwa P, Senthilselvan A, Dosman JA. CD14 gene variants and their importance for childhood croup, atopy, and asthma. Disease markers. 2013;35(6):765-71. https://doi.org/10.1155/2013/434920
6. Pawankar R, Canonica G, Holgate S, Lockey R, Blaiss M. WAO white book on allergy. Milwaukee, WI: World Allergy Organization. 2011;3:156-7. Available from: https://www.worldallergy.org/wao-white-book-on-allergy
7. Moses L, Morrissey K, Sharpe RA, Taylor T. Exposure to indoor mouldy odour increases the risk of asthma in older adults living in social housing. International Journal of Environmental Research and Public Health. 2019;16(14):2600. https://doi.org/10.3390/ijerph16142600
8. Rackemann FM. A working classification of asthma. The American Journal of Medicine. 1947;3(5):601-6. https://doi.org/10.1016/0002-9343(47)90204-0
9. Johansson S, Hourihane JB, Bousquet J, Bruijnzeel-Koomen C, Dreborg S, Haahtela T, Kowalski M, Mygind N, Ring J, Van Cauwenberge P. A revised nomenclature for allergy: an EAACI position statement from the EAACI nomenclature task force. Allergy. 2001;56(9):813-24. https://doi.org/10.1111/j.1398-9995.2001.00002.x-i1
10. Miranda C, Busacker A, Balzar S, Trudeau J, Wenzel SE. Distinguishing severe asthma phenotypes: Role of age at onset and eosinophilic inflammation. Journal of Allergy and Clinical Immunology. 2004;113(1):101-8. https://doi.org/10.1016/j.jaci.2003.10.041
11. Global Strategy for Asthma Management and Prevention. Global initiative for asthma [Internet]. 2020 [cited June 18, 2020]. Available from: https://ginasthma.org/gina-reports/
12. Shida A, Ikeda T, Tani N, Morioka F, Aoki Y, Ikeda K, Watanabe M, Ishikawa T. Cortisol levels after cold exposure are independent of adrenocorticotropic hormone stimulation. Plos one. 2020;15(2):e0218910. https://doi.org/10.1371/journal.pone.0218910
13. Malomgré W, Neumeister B. Recent and future trends in blood group typing. Analytical and Bioanalytical Chemistry. 2009;393(5):1443-51. https://doi.org/10.1007/s00216-008-2411-3
14. Wisamkadhum H. Study of Plasma Malondialdehyde, Albumin and Bilirubin Levels in Asthmatic Patients as Markers of Oxidative Stress. Al-Mustansiriyah Journal of Science. 2011;22(6). Available from: https://www.iasj.net/iasj/article/87381
15. Al-Smaism MF, AL-Sharify AN, Khurshaid RS. Evaluation of Enzymatic and Non Enzyme Antioxidants From Sera of Asthmatic Patients in Hilla City. Medical Journal of Babylon. 2014;11(3). Available from: https://www.iasj.net/iasj/download/05612ef506302497
16. Li CY, Erickson SR, Wu CH. Metformin use and asthma outcomes among patients with concurrent asthma and diabetes. Respirology. 2016;21(7):1210-8. https://doi.org/10.1111/resp.12818
17. Senna G, Latorre M, Bugiani M, Caminati M, Heffler E, Morrone D, Paoletti G, Parronchi P, Puggioni F, Blasi F, Canonica GW, Paggiaro P. Sex Differences in Severe Asthma: Results From Severe Asthma Network in Italy-SANI. Allergy Asthma Immunol Res. 2021;13(2):219-28. https://doi.org/10.4168/aair.2021.13.2.219
18. Abed RI. Quality of Life of Asthmatics Patients at Baghdad Teaching Hospitals. kufa Journal for Nursing sciences. 2016;6(2). Available from: https://www.iasj.net/iasj/article/114598
19. Salman AA, Al-Janabi BAS, Marbut MM. Epidemiological characters of Asthma in adult patients attending primary health care center in Dour city. The Medical Journal of Tikrit University. 2006;1(121):1-4. Available from: https://www.iasj.net/iasj/download/3d0b5d81ba076e86
20. Atiyah HH. Determination of Physical Problems for Adult Patients with Asthma. Mosul Journal of Nursing. 2013;1(2):48-53. Available from: https://mjn.mosuljournals.com/article_162919.html
21. Al-Jahdali H, Wali S, Salem G, Al-Hameed F, Almotair A, Zeitouni M, Aref H, Nadama R, Algethami MM, Al Ghamdy A, Dihan T. Asthma control and predictive factors among adults in Saudi Arabia: Results from the Epidemiological Study on the Management of Asthma in Asthmatic Middle East Adult Population study. Ann Thorac Med. 2019;14(2):148-54. https://doi.org/10.4103/atm.ATM_348_18
22. Crump C, Winkleby MA, Sundquist J, Sundquist K. Risk of asthma in young adults who were born preterm: a Swedish national cohort study. Pediatrics. 2011;127(4):e913-e20. https://doi.org/10.1542/peds.2010-2603
23. Canöz M, Erdenen F, Uzun H, Müderrisoglu C, Aydin S. The relationship of inflammatory cytokines with asthma and obesity. Clinical and Investigative Medicine. 2008:E373-E9. Available from: https://cimonline.ca/index.php/cim/article/view/4924
24. Elsayed W, Essa E. Iron deficiency anemia, serum iron in children with bronchial asthma. Zagazig university medical journal. 2017;23(1):1-11. https://dx.doi.org/10.21608/zumj.2017.4682
25. Hailemaryam T, Adissu W, Gedefaw L. Hematological profiles among asthmatic patients in southwest ethiopia: a comparative cross? section study. Hematol Transfus Int J. 2018;6(2):75-80.
26. Shin YS, Liu JN, Kim J-H, Nam Y-H, Choi GS, Park H-S. The impact of asthma control on salivary cortisol level in adult asthmatics. Allergy, asthma & immunology research. 2014;6(5):463-6. https://doi.org/10.4168/aair.2014.6.5.463
27. Chen E, Miller GE. Stress and inflammation in exacerbations of asthma. Brain, Behavior, and Immunity. 2007;21(8):993-9. https://doi.org/10.1016/j.bbi.2007.03.009
28. Taylor B, Mannino D, Brown C, Crocker D, Twum-Baah N, Holguin F. Body mass index and asthma severity in the National Asthma Survey. Thorax. 2008;63(1):14-20. https://doi.org/10.1136/thx.2007.082784
29. Muhammed SM, Sultan KM, Abdulrazaq MY. Asthma in Adults; Epidemiology, Risk Factor and Patterns of Presentation: A Cross Sectional, Questionnaire Based Study in Baghdad Teaching Hospital. Kerbala Journal of Medicine. 2012;5(11):1255-61. Available from: https://iraqjournals.com/article_64390_0.html
30. Tomlinson J, McMahon A, Chaudhuri R, Thompson J,

Wood S, Thomson N. Efficacy of low and high dose inhaled corticosteroid in smokers versus non-smokers with mild asthma. Thorax. 2005;60(4):282-7. https://.doi.org/10.1136/thx.2004.033688

31. Torén K, Murgia N, Schiöler L, Bake B, Olin A-C. Reference values of fractional excretion of exhaled nitric oxide among non-smokers and current smokers. BMC Pulmonary Medicine. 2017;17(1):118. https://doi.org/10.1186/s12890-017-0456-9

32. Liu T, Valdez R, Yoon PW, Crocker D, Moonesinghe R, Khoury MJ. The association between family history of asthma and the prevalence of asthma among US adults: National Health and Nutrition Examination Survey, 1999–2004. Genetics in Medicine. 2009;11(5):323-8. https://doi.org/10.1097/GIM.0b013e31819d3015

33. Bijanzadeh M, Ramachandra NB, Mahesh PA, Savitha MR, Manjunath BS, Jayaraj BS. Lack of Association Between Asthma and ABO Blood Group. Lung. 2009;187(6):389-92. https://doi.org/10.1007/s00408-009-9175-1

34. Kauffmann F, Frette C, Pham Q-T, Nafissi S, Bertrand J-P, Oriol R. Associations of blood group-related antigens to FEV1, wheezing, and asthma. American journal of respiratory and critical care medicine. 1996;153(1):76-82. https://doi.org/10.1164/ajrccm.153.1.8542166

35. Khetsuriani NG, Gamkrelidze AG. Erythrocyte antigens as immunogenetic markers of respiratory atopic diseases in Georgians. Journal of investigational allergology & clinical immunology. 1995;5(1):35-9. Available from: http://europepmc.org/abstract/MED/7551203

36. Mozalevskiĭ AF. [Polymorphic blood systems in children with bronchial asthma]. TSitologiia i genetika. 1985;19(3):220-5. Available from: http://europepmc.org/abstract/MED/3927538

37. Koers WJ, Houben GF, Berrens L. Blood groups ABO and grass-pollen hayfever. Allergie und Immunologie. 1989;35(3):167-72. Available from: http://europepmc.org/abstract/MED/2816665