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# ASTHMA AGREVATING FACTORS

**Dr. Rokan M. Fadhil***

***Corresponding Author: Dr. Rokan M. Fadhil**

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## SUMMARY

This study was carried out to determine the microbiological and immunological aspect of the two main asthma aggravating factors namely respiratory tract infection (bacteria and fungi) and exposure to allergen in baquba city.One hundred-thirty five patients, with asthma exacerbation were selected from patients attending the respiratory consultant unite through out aperiod extended for 8months. The age of patients ranged from (5-65) years with mean (28.85) years.Only one hundred patients were subjected to full assessment Bacteria were isolated from 13 (13%) patients, *Haemophilus influenzae* was the most common bacterial pathogen, which was isolated from 5(35.7%) patients, followed by *Streptococcus pneumonia*, which was isolated from 4 (28.7%) patients, *Moraxella catarrhalis*, which was isolated from 2 (14.3%) patients, *Pseudomonas arogenosa*, which was isolated from 2 (14.3%) patients, and *Niesseria species*, which was isolated from 1 (7%) patients and there was no significance correlation between growth (bacterial or fungal) and severity of asthma (P. >0.05).Fungi isolated from 9 patients (9%), and the most common fungal pathogens isolate were *Candida albicans*, which was isolated from 5 (55.6%) patients, followed by *Pencillium species*, which was isolated from 2 (22.2%) patients, *Aspergillus niger*, which was isolated from 1 (11.1%) patient, and *Aspergillus fumigatus* which was isolated from 1 (11.1%) patient and there was significant correlation (P<0.05) between steroid administration and fungal infections.Skin test was done to determine the commonest allergen, and blood samples were taken to determine the total IgE level. Twenty-five healthy subjects were used as a control group to determine the normal value of total IgE, and allergenisty to common allergens.Skin test for common allergen was positive in 70% of the patients and there was a significant correlation between asthma and skin test (P<0.05). The commonest allergen asthmatic patients sensitive to it was house dust mites, which was detected in (53%) of patients, followed by Barmoda grass pollens, which was detected in (41%) of patients and (34%) of patients were sensitive to at least one fungal allergen.The highest sensitization rate for fungal allergen was for *Candida albicans* (23%) followed by *Aspergillus fumigatus* (21%), *Helminthosporium halodes* (19%), *Cladosporium herbarum* (16%), *Alternaria tenius* (15%), and *Pencillium notatum* (14%). The highest sensitization rate for mould was at young age group (5-15) years old. Skin test was positive more frequent in patients with early onset asthma than patients with late onset asthma, while it was negative more frequent in patients with late onset asthma than patient with early onset asthma and the difference was significant, (P<0.05).Eighty two percentage (82%) of patients had elevated total IgE level above (100 I.U./ml), and the mean S.D. was (333.3 47.44), while in control group only (20%) of subject had IgE level above (100 I.U/ml), and the mean SD was (64 17). And the difference was significant (P<0.05). Also, the total IgE level for asthmatic patients with positive skin test was higher than total IgE level for patients with negative skin test, and the difference was significant (P<0.05). **Aims of the Study:** Determine the role of micro-organisms (bacteria and fungi) in asthma exacerbation.

. Determine the prevalence of sensitivity to common allergens in asthmatic patients.

. Determine the relationship between total IgE level and asthma.

. Determine the relationship between skin test and asthma.

## INTRODUCTION

Asthma is the most common cause of long terms respiratory disease, which affecting approximately (5-10%) of population (Anderson et al., 1988).The risk factors associated with the development of asthma have been the focus of many investigators.

in the last two decades (Morgan and Martinez 1992). Although viral respiratory infections are important triggers of acute exacerbation of Asthma (Weiss *et al.*, 1985), the role of bacteria is less clear and acute bacterial exacerbation are frequent problems in the management of asthma (Chodosh, 1985). There are number of pathological abnormalities of the bronchial system in asthmatic patients. These include impaired mucociliary clearance, bronchial obstruction, resident infestation of the bronchial epithelium with bacteria, and even normal ciliated epithelium cannot clear the excessive and abnormal secretions present (Chodoshi, 1985). There is a good evidence that Hamophillas inflauenzae persist in the bronchial epithelium and provide a reservoir for acute bacterial exacerbation wherever host defense

mechanisms are compromised (Hjuler, 1995).In addition, clinicians are faced with a problem of identifying patient who require antibiotic therapy during such an exacerbation most physicians include an antibiotic in the treatment regimen for exacerbation of bronchospasm (Editorial, 1987), the decision to do so is influenced by several factor amongst which bacterial cultures are important. Not with standing it's disadvantages sputum culture is the main method to determine the presence of bacteria in respiratory tract (Moser, 1991) and is widely used in clinical practice. However, cultures take-up to 48 hours and there is no other simple method to identify the patients who have positive cultures at the time of admission or visit since this could influence empirical antibiotic usage. A preliminary study with a case control design was undertaken to ascertain whether certain variable were associated with sputum positivity (outcome) and whether clues derived thus could be incorporated into clinical practice.Approximately 12% of asthmatic children undergoing an exacerbation have sputum cultures, which are compatible with bacterial infection (De Blic, 1982). The most frequently identified bacteria are the following: ***Heamophilus inflaunzae, Moraxella Catarrhalis, Streptococcus Pneumonia, Mycoplasma Pneumonia and Staph. aureus*** (Fayon, 1999). Many children may be colonized by potentially pathogenic bacteria in their upper airway (Hjuler, 1995) and so the diagnosis of bacterial infection is difficult to confirm in the absence of lower respiratory tract quantitative cultures.Antimicrobial therapy has not been shown to be of clinical utility in children with acute asthma (Shaprio, 1974 and Graham, 1982). Interestingly; these studies have excluded patients with pneumonia or bacterial infection. The usual cause of acute bronchitis and exacerbation of asthma are viral infection of upper air ways including ***Influenza A*** and ***B, Parainflaunzae, Coronovirus, Rhinovirus,*** and ***Respiratory syncytial virus*** (Gonzales and Saudi, 1995). house hold dust mites produce one of the most common indoor allergens and exposure to dust mite is a major risk factor for development and exacerbation of asthma (Platts-Mills, 1989). There are different types of household dust mites in different geographic areas but all most commonly resident in carpets, pillows, mattress and soft furnishing (Platts-Mills, 1994). Mold and other fungi are other common indoor allergen and out door allergen responsible for asthma exacerbation the optimal environment for fungi to grow is in dark damp and poorly ventilated places such as basements.

## MATERIALS AND METHODS

**Patients:** This study included 135 asthmatic patients with asthma exacerbation attending therespiratory unite in baquba teaching hospital. The age range was 5-65 years with mean of (28.85 + 15.57). A total of 25 healthy individual with age range from 7 to 60 years where examined as a control group, for evaluation of the normal total IgE value and the prevalence of skin test for common allergens .One hundred patients (74%) were taken in full assessment, careful detailed history, physical examination, chest X ray, complete blood picture, stool and urine analysis to exclude parasitism, and pulmonary function test were carried out. Skin test was performed to determine sensitivity to common allergens, and sputum samples were collected for bacterial and fungal culture. Blood samples were collected for total serum IgE level assessment (Elisa).

## METHOD

Patients were instructed to expectorate the sputum, try forceful cough two to three times, and the sputum was collected in a sterile universal plastic container. Most of the sputum specimens were dealt with one hour after collection. Specimens, which are not handled within this time, it was kept in the refrigerator at approximately 4C°but not more than 1-3 hours (Baron and Finegold 1990).

Gram's stain was performed to a purulent portion of each sputum specimen and examined microscopically for culture suitability and for a presence of fungal element under low power. Samples were considered of good quality if they had <10 squamous cells and >25 leukocytes pear low-power field (Sanguinetti *et al*., 2000). Otherwise, the sputum sample was considered contaminated by saliva and rejected. Good quality specimens were screened for a predominant bacterial morphological type under oil immersion field (X100). A predominant morphotype was defined as a presence of a single morphotype that accounted for > 75% of organisms seen (Sanguinetti *et al*., 2000). A loopfull of purulent portion of each sputum sample was inoculated directly on blood, chocolate, macConeky's and Sabouraud's agars (with Chloramphenicol and cyclohexamide, and with Chloramphenicol only). Blood agar plates were incubated aerobically.

Chocolate agar plates were incubated in 5-10% Co2 (GAS generating kits, oxide, England).while MacConeky's agar plate was incubated aerobically.All plates (except Sabouraud's agar plates) were incubated at 37C° for 24 hours and then examined for bacterial growth. Plates showed no growth after 24 hours were further incubated for another 24 hours before discarding them as negative (Finegold & Martin 1982).Sabouraud's agar plate incubated at room temperature, and held for 30 day before discarded as negative, humidity were maintained in the incubators by placing an open pan of water under a button shelf. Culture examined daily during the first 2 weeks of incubation, then twice weekly schedule thereafter (Koneman & Roberts 1985). Diagnosis was considered presumptive when predominant microorganism isolated from a purulent sample (presence of >25 polymorphoneuclear leukocytes and <10 Sequamous cells per low magnification field [X10]) and the findings of gram staining were compatible (Rosou *et al*., 2001).

***Identification of isolated organisms:*** Bacterial identification was based on morphological

(microscopically and macroscopically depending on colonies morphology) and biochemical (Api test) characteristics.

Yeast identification was based on morphological and biochemical characteristic, while mold identification was based on morphological characteristic (Koneman & Roberts, 1985). It is generally possible to determine from visual examination whether a fungal colony is a mold or yeast, mold colonies have fuzzy or stringy appearance from the growth of aerial hyphae.

***Determination of total IgE level:*** Total IgE level determined by direct enzyme linked immunosorbent assay kit.

***Determination of allergens:*** The types of allergens, the patient sensitive to it were determined by skin testing to commonest allergens, which was performed when the patients free from asthmatic attack.

***Statistical analysis:*** The data collected were analyzed using computer facilities with version 10 (statistical package for social science).Data were presented in simple measure of frequency, percentage mean and stander deviation. Significance of difference was tested using chi-square (X2), P value <0.05 is considered significant. Depending on the clinical presentation of patients; sputum were taken to be examined and cultured for the identification of the causative agents. Blood samples were collected for the determination of total serum IgE level, and skin test was done to determine the prevalence of common allergens.

## RESULTS

A total of (135) patients with infectious asthma were included in the present work. Only one hundred patients received full assessment.The mean age of patients was (28- 85 15.57) ranged from (5-65) years old. The higher occurrence of asthma exacerbation was at age group (5-15) years as shown in table (1).

**Table. (1): Age and sex distribution of patients.**

| Age | Males | | Females | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| 5-15 | 18 | 18 | 7 | 7 | 25 | 25 |
| 16-25 | 14 | 14 | 7 | 7 | 21 | 21 |
| 26-35 | 4 | 4 | 12 | 12 | 16 | 16 |
| 36-45 | 6 | 6 | 10 | 10 | 16 | 16 |
| 46-55 | 6 | 6 | 7 | 7 | 13 | 13 |
| 56-65 | 4 | 4 | 5 | 5 | 9 | 9 |
| Total | 52 | 52 | 48 | 48 | 100 | 100 |

Out of 100 patients studied with asthma exacerbation 17 (17%) patients had positive culture (bacterial and/or fungal), 8 (47%) patients had bacterial infections only, 4 (24%) had fungal infections only and 5 (29%) had mixed growth, as shown in figure (1).

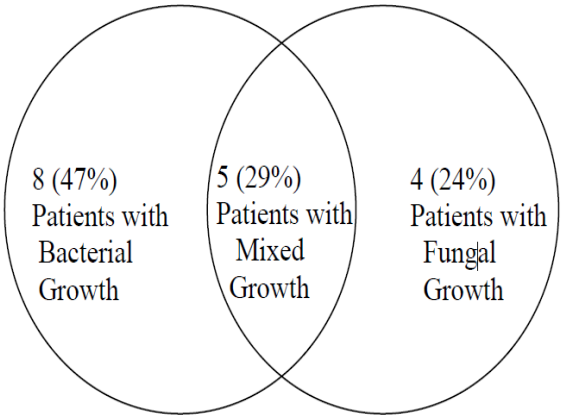



**Figure. (1): Distribution of major etiological agents (bacteria and fungi) of infectious asthma in 100 patients.**

Table 2 show that Among 100 patients with asthma 13 (13%) patients gave positive bacterial pathogens growth, from them 12 (92%) patients had infections with single bacterial pathogens and only one patients (8%) had 2 bacterial pathogens, so that the total number of bacterial pathogens isolated were 14 isolates.The most frequently isolated bacteria was ***H. influenzae*** which was isolated from 5 (35.7%) patients,

**Table. (2): Number and percentage of bacterial pathogens isolated.**

| Bacterial pathogens | No. | %* |
|---|---|---|
| ***H. inflaunzae*** | 5 | 35.7 |
| ***S. pneumoniae*** | 4 | 28.7 |
| ***M. catarrhalis*** | 2 | 14.3 |
| ***P. arogenosa*** | 2 | 14.3 |
| ***Niesseria spp*** | 1 | 7 |
| Total | 14 | 100 |

*(%) was calculated to the total number of bacterial pathogen isolated.

Table (3) shows that from 13 (13%) patients with bacterial growth 7 (54%) patients were on steroid and the remaining 6 (46%) patients non steroid user, while from 87 (87%) patients with no bacterial growth 29 (34%) patients were on steroid and the remaining 58 (66%) patients were non steroid user and the difference was non significance (P value >0.05.

**Table (3): Relationship between bacterial infection and steroid administration.**

| Steroid Administration | Growth* No. and (%) of Patients | No Growth* No. and (%) of Patients |
|---|---|---|
| Non steroid | 6 (46) | 58 (66) |
| On Steroid | 7 (54) | 29 (34) |
| Total | 13 (100) | 87 (100) |

*P value = 0.131*
*Growth* = Bacterial growth*

From 17 patients with positive culture (bacteria and/or fungi), 8 patients (47.06%) had sever type of asthma, while from 83 patients with negative culture (bacteria and/or fungi) 52patients (62.66%) had sever type of asthma, and the difference was non significant (P value >0.05), as shown in table (4).

**Table 4: Frequency of microorganism (bacteria and/or fungi) in relation to severity.**

| Severity | Growth* No. and (%) of Patients | No Growth* No. and (%) of Patients |
|---|---|---|
| Mild | 9 (52.94) | 31 (37.34) |
| Sever | 8 (47.06) | 52 (62.66) |
| Total | 17 (100) | 83 (100) |

*P value =0.177*
*Growth* = Bacterial and/or fungal growth*

Table 5: shows that Fungi were isolated from sputum samples of 9 (9%) patients. And the commonest fungal pathogens was *C. albicans*.

**Table. (5): Number and percentage of fungi isolated.**

| Fungi | No. | %* |
|---|---|---|
| ***Candida albicans*** | 5 | 55.6 |
| ***Pencillium spp*** | 2 | 22.2 |
| ***Aspergillus niger*** | 1 | 11.1 |
| ***Aspergillus fumigates*** | 1 | 11.1 |
| Total | 9 | 100 |

*(%) was calculated to the total number of fungi isolated.

Table 6) shows the relationship between fungal infections and steroid administration. From this table we noticed that fungal infections were higher among asthmatic patients on steroid and the difference was significant(p value <0.05).

**Table (6): Relationship between fungal infection and steroid Administration**

| Steroid Administration | Growth* No. and (%) of Patients | No Growth* No. and (%) of Patients |
|---|---|---|
| Non Steroid | 2 (22) | 62 (68) |
| Steroid using | 7 (78) | 29 (32) |
| Total | 9 (100) | 91 (100) |

*P value =0.01*
*Growth* = Fungal growth*

Table (7) shows that fungal infections were more frequent in asthmatic patients taking steroid for long duration and the difference was non significant, p value >0.05.

**Table. (7): Relationship between duration of steroid administration and fungal infection in.**

| Duration | Growth* No. and (%) of Patients | No Growth* No. and (%) of Patients |
|---|---|---|
| Less than 5 years | 2 (28) | 18 (62) |
| More than 5 years | 5 (72) | 11 (38) |
| Total | 7 (100) | 29 (100) |

*P value =0.120*
*Growth* = fungal growth*

Results of skin test to common allergen were positive in (70%) of the patients, while in healthy control group was positive in (12%) only, and the difference was highly significant, (P value <0.001), as shown in table (8).

**Table. (8): Skin test reactivity in asthmatic patients and control group.**

| Skin Test Reactivity | Asthmatic Patients | Control Group |
|---|---|---|
| Positive skin test | 70 (70%) | 3 (12%) |
| Negative skin test | 30 (30%) | 22 (88%) |
| Total | 100 (100%) | 25 (100%) |

*P value <0.001*

From history taking we notice that earlier onset is significantly obvious in positive skin test group, table (9) and figure (2), shows proportion of asthmatics with age at onset of asthma, (92%) of patients who had the disease before 10 years of age are skin test positive and (76%) of patients who developed the disease in 10-20 years of their age are skin test positive while only (33%) of patients who had the disease after the second decade of their life are skin test positive to at least one allergen in the panel of skin test and the difference was highly significant, (p value <0.001).

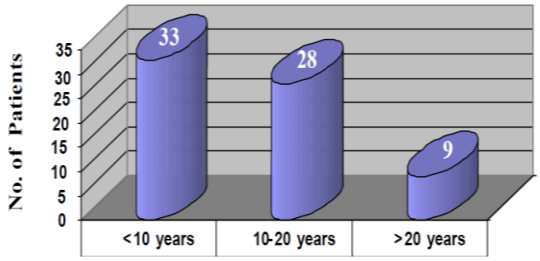
**Table. (9): Distribution of asthmatic patients according to skin test reactivity and age at onset.**

| Age at Onset | Skin Test Positive n=70 No. and (%)* | Skin Test Negative n=30 No. and (%)* | Total No. and (%)* |
|---|---|---|---|
| <10 years | 33 (92) | 3 (8) | 36 (100) |
| 10-20 years | 28 (76) | 9 (24) | 37 (100) |
| > 20 years | 9 (33) | 18 (67) | 27 (100) |

*P value <0.001*
** (%) Calculated to the total No. of patients at that age interval of onset.*

Distribution of our patients according to skin test reactivity is shown in figure (3) A and B).

**(A)** Skin test positive patients (n=70).




**(B)**

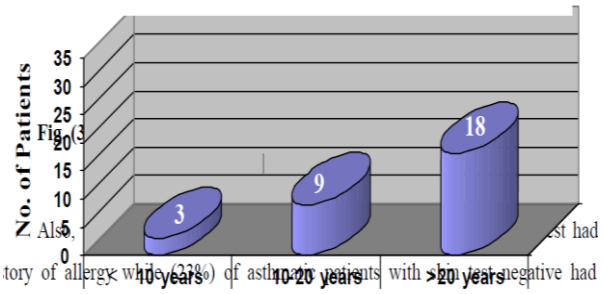



**Fig. (3.4, A and B): Distribution of the asthmatic patients according to skin test reactivity and age at onset.**

Also, we found that (51%) of asthmatic patients with positive skin test had family history of allergy while (23%) of asthmatic patients with skin test negative had family history of allergy.

Table (10) show that HDM was the commonest allergen, the patients were sensitive to it, which was detected in (54%) of patients and (4%) of control.

**Table (10): Prevalence of common allergen in asthmatic patients.**

| Allergen | No. | % |
|---|---|---|
| HDM | 54 | 54 |
| Grass pollen | 41 | 41 |
| Fungal allergens | 34 | 34 |

Table( 11) shows that sensitivity to HDM was most frequent in patients with asthma alone (63%) than in patients with asthma in association with other allergic conditions.

**Table. (11): Prevalence of common allergens in patients with asthma alone and patient with asthma in association with other allergic disease.**

| Allergens | Asthma n=30 No. and (%)** | Asthma +AD*** n=2 No. and (%)** | Asthma +AR**** n=53 No. and (%)** | Asthma +AD+AR n=15 No. and (%)** | Total No. and (%) * |
|---|---|---|---|---|---|
| HDM | 19 (63%) | 1 (50%) | 27 (50.9) | 7 (46.7) | 54 (54) |
| Grass | 13 (43.3) | 1 (50) | 20 (37.7) | 7 (46.6) | 41 (41) |
| Mold | 11 (36) | 0 | 19 (35.8) | 4 (26.6) | 34 (34) |

*Calculated to the total number of patients (100).** (%) Calculated to the number of patients had that type of allergic disease.*** AD = Atopic dermatitis.**** AR = Alergic rhinitis.*

Table 12show that Sensitivity to mold was more frequent in age group (5-15) years (76%) and then start to declan sharply with age.

**Table (12): Pattern of allergensity to fungal allergen in relation to age.**

| Age | No. | %* | %** |
|---|---|---|---|
| 5-15 | 19 | 76 | 19 |
| 16-25 | 9 | 42 | 9 |
| 26-35 | 3 | 18 | 3 |
| 36-45 | 2 | 12 | 2 |
| 46-55 | 1 | 7 | 1 |
| 56-65 | 0 | - | - |

** (%) Calculated to the total number of patients at that age group.** (%) Calculated to the total number of patients (100).*

The most frequent fungal allergen the patients were sensitive to it was ***C. albicans***, which was detected in 23 (23 %) patients.

**Table (13): Pattern of allergensity to different types of fungal allergens (mold).**

| Fungal Allergens | No. | % |
|---|---|---|
| *C. albicans* | 23 | 23 |
| *Aspergillus fumigates* | 21 | 21 |
| *Helminthosporium halodes* | 19 | 19 |
| *Cladisporium herbarum* | 16 | 16 |
| *Alternaria tenius* | 15 | 15 |
| *Pencillium notatum* | 14 | 14 |

Total IgE levels for asthmatic ranged from (75 to 3500) I.U/ml with mean of (333.3 □47.44), while in control group, their IgE level ranged from (5-115) I.U/ml with mean of (64 μ17)table 16.

**Table (14): Distribution of total IgE level of asthmatic patients and control.**

| Total IgE level | Asthmatic patients No. and (%) | Control group No. and (%) |
|---|---|---|
| Below 100 I.U/ml | 18 (18) | 20 (80) |
| 100-500 I.U/ml | 57 (57) | 5 (20) |
| 500-1000 I.U/ml | 16 (16) | 0 (0) |
| Above 1000 I.U/ml | 9 (9) | 0 (0) |
| Total | 100 (100) | 25 (100) |

If the level of 100 I.U/ml is adapted as the upper limit of normal IgE level we notes that 18 (18%) patients had IgE level below 100 I.U/ml and 82 (82%) patients above 100 I.U/ml, while in control group 20 (80%) had IgE level below 100 I.U/ml and 5 (20%) had IgE level above 100 I. U/ml, and the difference was significant, (P value <0.05) as shown in table (15).

**Table. (15): Comparativ statistic between IgE level Of asthmatic patients and control.**

| IgE level | Asthmatic patients No. and (%) | Control group No. and (%) |
|---|---|---|
| Below 100 I.U/ml | 18 (18) | 20 (80) |
| Above 100 I.U/ml | 82 (82) | 5 (20) |
| Total | 100 (100) | 25 (100) |

Table (16) shows that 67 (96%) had IgE level above 100 IU/ml, while for skin test negative patients 15 (50%) patients had IgE level above 100 I.U/ml, and the difference was significant, (P value <0.05).

**Table (16): Comparison between IgE level of skin test positive asthmatic and skin test negative asthmatic.**

| IgE Level | Skin Test Positive No. and (%) | Skin Test Negative No. and (%) |
|---|---|---|
| Below 100 I.U/ml | 3 (4) | 15 (50) |
| Above 100 I.U/ml | 67 (96) | 15 (50) |
| Total | 70 (100) | 30 (100) |

*P value <0.05*

## DISCUSSION

Asthma aggravating factors are divided into two categories, allergic (e.g. exposure to allergen) and non-allergic (e.g. respiratory tract infection) (Shobokshi, 2000).Kornohen *et al*., (2001), submit that the common exacerbating factor for asthma are:

1. Respiratory tract infections (63%).
2. Exposure to allergens (24%).
3. Unknown (or others) (13%).

Both exposure to allergen and respiratory tract infection especially viral respiratory tract infection have been recognized to be important triggers of asthma exacerbation but the possible interaction of these has been not assessed in an epidemiological study, (Tarlo *et al*., 2001).

Esposto and Princip, (2001), reported that asthma etiology is complex, involving interactions between genetic susceptibility, allergen exposure and external aggravating factors such as air pollution, smoking and respiratory tract infections. In the present study we found that infective exacerbation of asthma were more frequent in age group (5-15) years, which 41 (30%) patients located at this age group, this result is in agreement with other studies (Teichtahl *et al*., 1997; Kornohen *et al*., 2001), the possible explanation for this is that the respiratory tract infections exacerbate asthma in children more frequent than adult because of small size of bronchi in children, in addition to that respiratory tract infection is common in children, because of there low immunity and mixing with other children in school. At the same time, in children the occurrence of infectious asthma were higher in male (18%) than female (7%), this perhaps may be due to lung size, boys generally have smaller lungs than girls, also may be due to greater susceptibility to viral infections in males as they may be exposed to outdoor airborne infection more frequent than females (El-Gamal *et al*., 1993).Respiratory infections precipitate wheezing in many asthmatic patients and may be involved in aetiopathogenesis of asthma. Several studies had demonstrate that viral infection exacerbate asthma. Bacterial and fungal infections had been so overlooked, emphasis is put in the viral infections, but bacterial infection usually associated with it was ignored.

Several studies were under taken in the past to define the role of infection in exacerbation of asthma. Since early 1950's evidence for sputum cultures for bacterial infection especially, ***H. influenzae*** and ***S. pneumonia***

has been found in few asthmatic exacerbation (Busse, 1990) yet there were many difficulty which has been encountered in ascribing a pathogenic role to bacteria in acute symptomatic deterioration, because.

1. There was big chance of contamination of sputum samples with upper respiratory flora which contain even potentially pathogenic bacteria colonizing upper respiratory tract, even when sample collected by transtrachial aspirate there was (3.4%) chance of contamination with upper respiratory tract flora, (Fayon *et al*., 1999).

2. Potentially pathogenic bacteria may be cultured from sputum or trastrachial aspirate obtained from asthmatic patients in between attack, colonizing lower respiratory tract (Khalifa *et al*, 1993), so the diagnosis of bacterial infection is difficult to confirm.On the other hand clinical deterioration may occur with no significant growth on culture, and even if positive may not reflect an infection on serology therefore it is doubtful whether a positive sputum culture signifies infection, hence the term respiratory infection has been carefully avoided through out this study, so it is presumptive diagnosis. Also, in some apparently purulent sputum when do wet film we saw eosenophile not neutrophile. In present study among one hundred patients only 13 (13%) patients gave positive bacterial culture, this result is in agreement with other findings (Kraflin, 2000; Shimada *et al*., 2001), the efficacy of antibiotic therapy is also unclear and even more controversial of the acceptable trails, the majority have found no benefits from antibiotic therapy,(Sachs, *et al*., (1995) reported that antibiotics given with a short course of oral predniselone during an exacerbation do not accelerate recovery as measured by changes in peak flow and symptom, scores in ambulatory patients with mild to moderate asthma or COPD when treated by their general practitioners. More over, antibiotic do not reduce the number of relapses after treating an exacerbation, so that the main bacterial infections have no or minimum role in exacerbation of asthma. This would suggest that sputum production alone should not be regarded as evidence of microbial infections and does not support the widespread use of antibiotics in uncomplicated asthmatic patients.The commonest bacteria isolated was ***H. inflaunzae*** 5 (35.7%), this result in agreement with other studies done ( Fayon 1999; Shimada *et al*., 2001). The slight difference in percentage of infections with these microorganisms in different studies referred to the microbiological technique used for collection of sputum sample and isolation of microorganism and preparation of patients.In this study ***P. aeruginosa*** detected in 2 patients both of them are on systemic steroid for long duration, this result coincide with other finding by (Nadel *et al*., 1998).

Bacterial infection exacerbate asthma by many ways, Huang and Zhong, (1993) stated that pathogenic bacteria that produce respiratory tract infections and exacerbate asthma release histamine both in vivo and vitro, which is an inflammatory mediator that causes bronchospasm. Pauwels *et al*., (1980) detected IgE antibodies in (24%) of asthmatic patients, and he concluded that immediate hypersensitivity to bacteria may play a role in the infective exacerbation of bronchial asthma. Steroid is one of drugs commonly used in management of asthma and as we know this drug decrease immunity and predispose patients to infection. In the present study we found that there was no significant correlation (P>0.05) between steroid administration and bacterial culture positivity, although ***P. aeruginosa*** detected in 2 patients both of them on steroid but in general there was no significant correlation between bacterial infections and steroid administration. Also, there was no correlation between the severity of asthma and positive bacterial culture (p value >0.05), this result come in agreement with other results (Springer, 1992; Khalifa *et al*., 1993).

Fungal pathogens induced obstructive airway disease in atopic individuals can be differentiated into two categories, first uncomplicated asthmatic reactions, due to high but transient exposure to fungal spores (fungal asthma), resulting in a TH2 response with immunoglobuline E mediated reactions and eosinophil infiltration a second, more complex asthmatic reaction due to colonization of mucus epithelium surface by virulent protease producing fungi, the later condition stimulates as exaggerated immunological inducing all subclasses of antibodies directed against the micro-organism and intense eosenophilic infiltrate of the airway (Kuaffman *et al*., 1995). In this study among 100 patients with infectious asthma 9 (9%) patients gave positive fungal cultures, from them 4 (45.4%) patients had only fungal infection and the remaining 5 (55.6%) patients had mixed infection with bacteria and the commonest fungal isolates were ***C. albicans***, which was detected in 5 (55.6%) patients, this result was in agreement with others ( Kockovska, 1995; Ellepola *et al*., 2001). Bandele *et al*., (1993) There was a significant correlation (p value <0.05) between steroid administration and fungal infections and also, there was a correlation between duration of steroid administration and fungal infections, but not significant, this result comes in agreement with (Vogt, 1979; Toogood *et al*., 1980).In present study 70% of patients had skin test positive to common allergens, this coincides with result obtained by (Herbert *et al*., 1982; Zimmerman *et al*., 1988).In case history, age at onset is important because as found in this study, an earlier onset is usually associated with extrinsic asthma which is in agreement with; Inouye *et al*., 1985). Higher incidence of personal and family allergies were notably found in asthmatics with skin test positive, where it was about two times that than what appeared in negative skin test asthmatics, same as reported by (Hendrick *et al*., 1975; Inouye *et al*., 1985). There was a good association between the age at onset of asthma and the incidence of positive skin test, as we found higher incidence of positive skin test reactions in those with age less than 10 years at onset asthma, which is mostly of extrinsic (allergic or atopic) type. Than those who develop asthma

after that which is in agreement with (Hendrick *et al*., 1975; Tang and Iw, 1989).Association of skin test with history in this study showed that (74%) of patients with positive skin test had positive history to the allergen(s) appearing in their skin test and only (11%) negative skin test asthmatics gave a positive history which in agreement with (Hendrick *et al*., 1975).The commonest allergen, the patients were sensitive to it was HDM, which was detected in 53 (53%) patients. This result come in agreement with and intermediate to result of other series (; Ezeamusic, 2000; Chon *et al*., 2002; Leung *et al*., 2002).Fungus is known to be one of the causative allergens inducing bronchial asthma as are house dust mites and Barmoda Grass Pollen. Out door fungi such as ***Cladosporium***, ***Alternaria***, ***Pencillium*** and ***Aspergillus spp***. are important fungi that inducing IgE antibody formation and asthma exacerbation (Akigama, 2000).In the present study we found that (34%) of patients enrolled in this study were sensitive to at least one fungal allergen, this result is in agreement with finding of other studies (Ezeamuzic, 2000; Katz *et al*., 1999) keeping in mind that this study was done in Autumn and the incidence might had been affected by mold concentration in air, and this may explain the slight difference between our results and other studies.Patients with asthma and allergic rhinitis had the highest sensitization rate than patients with asthma alone. This result disagree with (Ezeamuzic, 2000) In this study we found that ***C. albicans*** and ***Aspergillus fumigatus*** Had the highest sensitization rates (23% and 21%, respectively) This result coincide with results obtained by (Ezeamuzic, 2000; Katz *et al*., 1999).Although ***C. albicans*** is known to induce TH1 clones that suppress IgE synthesis, serum IgE antibodies against ***C. albicans*** is often increase in atopic patients, In the present study we notice that sensitivity to mold decrease with age, the highest sensitization rate among patients in age group (5-15) years were (65%) and then decline sharply with age reaching the lowest sensitization rate at age group (46-55) and (56-65) were (7% and 0%), respectively. This result come in agreement with Ezeamuzic *et al*., (2000) and possible explanation for that was due to continuos exposure to fungal allergens may lead to decrease sensitization rate to it (Niedoszytko *et al*., 2002). In this study, the mean IgE level for asthmatic patients was (333.3 47.44), and this result approximate value reported by (Sureyya, 1994; Agha *et al*., 1997). Significantly higher IgE levels in asthmatic than control were found in our study, and in asthmatics who could have had the disease due to extrinsic factors (skin test positive) than asthmatics in whom extrinsic factors could not be as contributing for their asthma (skin test negative). This is consistent with (; Ikeda and Makinos, 1994; Kartasamita *et al*., 1994). ±

## CONCLUSIONS

1. Bacterial and fungal infections play minor role in asthma exacerbation.
2. Purulent sputum by morphology (or macroscopically) do not always means that there was pus cell because eosenophile infiltrate not neutrophile.
3. House dust mites were the commonest allergens in asthmatic patients sensitive to it.
4. Total IgE level have a significant correlation with asthma.

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