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Influence of Nasopharyngeal Microbiota on Pediatric Asthma: Insight from Case–Control Study in Holy Karbala, Iraq

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Abstract— Background: Asthma and the normal flora have a complicated interaction; research points to the potential importance of some commensal microbes in the development of asthma. Early life exposure to specific environmental microorganisms may be essential for the appropriate development of the immune system and the prevention of asthma. The host's immune system and microbiome interact to significantly impact the pathways that lead to the development of asthma. Methods: This is a case-control study. Nasopharngeal swabs and Sera were collected from Teaching children City in Holy Karbala, Iraq, during 2022-2023. Nasopharngeal swabs was culturing by culture media and diagnosed by VITEK2. Results: A case-control study involving 100 kids ages 1 to 5 was conducted. Of those, 50 kids had asthma, whereas the other 50 kids were in good health. All participants provided nasopharyngeal swabs, and the VITEK 2 system was used to identify the nasopharyngeal microbiome following primary organism isolation through standard cultures using various media, including blood agar, chocolate agar, macconkey agar, manitol salt agar. Subculture and gram stain are performed following each primary culture to differentiate gram positive (purple-colored) bacteria from gram negative (reddish-pink) microorganisms. Conclusion: A subset of children with sub recurrent wheezing who have asthma had a different micro biome composition than healthy controls. It was outside the purview of this study to determine if this difference is related to asthma development/severity/difficult and delayed treatment. the ultimate objective is to control and prevent asthma by regulating the micro biota.

***Index Terms*— pediatric asthma, nasopharngeal microbiota, exacerbation, VITEK2 method.**

1. Introduction

One of the most prevalent long-term respiratory conditions is asthma. Asthma symptoms, which are common and have significant effects on public health, include coughing, wheezing, shortness of breath, and chest tightness. These symptoms significantly interfere with children's and adults' everyday life and professional activities [1]. Of them, the prevalence of asthma is greater in high-income countries than in low-income countries [2]. Over the past few decades, research on the pathophysiology of asthma has been conducted, and the results show that the condition has multiple etiologies. Asthma is a complex, multifaceted illness that is influenced by various factors that contribute to its start and progression, such as genetic predisposition, environmental exposures, and host features, as numerous studies have shown [3].

An accumulating body of research indicates that asthmatics' microbiomes are different from those of healthy individuals. It is necessary to comprehend the relationships between pathogenic and helpful microorganisms as well as the associated immune-inflammatory responses in order to comprehend the pathophysiology of asthmatics [4]. The development of asthma is triggered by intricate processes that include subsets of regulatory T-cells and toll-like receptors, among other things. This pathway may be impacted by alterations in the microbiota's composition brought about by a range of lifestyle variables. In the late 1980s, Strachan introduced the "hygiene hypothesis," which postulated a connection between microbes and allergies [5]. The microbiomes of various anatomical locations are linked to one another and interact with one another, rather than having an independent effect on the development of asthma [6], [7].

A study on childhood asthma suggests that early life exposure to germs has a significant impact on the development of the immune system in children. In light of changes in contemporary lifestyles, such as an increase in the number of cesarean sections performed, an increase in the use of antibiotics, the widespread use of formula feeding, and changes in contemporary dietary patterns, all of which have a significant impact on the components of the gut microbiome, the original "hygiene hypothesis" has been further supported and improved [8], [9].

Recent research has linked lung and gut flora dysbioses to the development of the immune system; their relationship with the exacerbation of asthma is especially noteworthy [10]. Dysbiosis, or an imbalance in the distribution of resident microbial taxa, has been linked to asthma and other allergy and inflammatory illnesses. This relationship has been investigated utilizing cutting-edge scientific tools and interdisciplinary approaches [11]. In The relationship between the microbiome and human health and disease is becoming a prominent area of attention as scientific and technological developments expand our understanding of the microbiome. Human microbiota in

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good health is widely distributed [12].

About 827 nasal swabs from 47 infants were tested in a previous study, which was conducted every two weeks. The results showed an increase in microbial density within the first year of life, which was mirrored by a decrease in diversity. Individual differences in the microbiome suggest the existence of a modified respiratory microbiota [13]. Additionally, this study found that the microbiome of each individual is shaped by seasonality and age.

It's interesting to note that different asthma phenotypes show distinct changes in the nasal microbiome. A common core genera, such as Moraxella, Haemophilus, Staphylococci, and Streptococcus, were found in over 90% of the 163 children whose nasal microbiotas were assessed. However, Proteobacteria, Actinobacteria, Bacteroides, Corynebacterium, Dolosigranulum, and Prevotella varied significantly among asthma phenotypic clusters, indicating that respiratory microbiotas are useful biomarkers that could support clinical classification [14].

68 nasal swabs from the two groups were analyzed for this study, and the results showed a substantial difference in the microbial community between the asthmatic children and the healthy control group, with a prevalence of Moraxella and a lesser variety [15].

On the other hand, two other investigations found that children with asthma who had a nasal microbiota dominated by Staphylococcus had a decreased likelihood of experiencing exacerbations. [6], [7].

Aim of the study is to evaluate the association between the upper respiratory micro biome, with asthma severity, type, and control through the following objectives:

Firstly, to Identify the type of bacterial micro biome in the respiratory tract of children with asthma and in healthy control children. Secondly to Correlate specific bacterial microbiota growth with asthma severity, type, and control.

2. Methods

A. Studying group

This case- control study was done at children's teaching hospital in Karbala. All patients collected were registered in respiratory center in hospital from August (2023) to January (2024). Patients: 50 patients randomly recruited from the teaching children hospital in Karbala, who are diagnosed to have asthma based on clinical and laboratory findings) lymphocyte, neutrophils, eiosinophils) by the pediatrician. Controls: Healthy controls, 50 children .With matched age and sex to the patients' group.

Inclusion criteria:

Patients' inclusion criteria were age 1-5 years old; both sexes, diagnosed as asthma\recurrent wheezer. Classification of asthma severity, type of asthma, and control of asthma will depend on the pediatrician.

Exclusion criteria:

Patients were excluded if infection in the respiratory tract is suspected, antibiotic treatment up to 2 weeks ago, any other inflammatory or autoimmune diseases, and patients on drugs with immunosuppression.

B. Methods

A-Patient data: Demographic and Clinical data will be collected using a specific detailed questionnaire.

B-Sample collection: 1. Nasopharyngeal swabs will be taken from each subject. Before being shipped to the lab on ice, the swab will be put in gel transport media and chilled at 2–8 °C. The swab will be taken out when the sample arrives at the microbiology lab, and standard bacterial cultures (i.e., streaked plates using the proximal part of the swab) will be conducted. 2. Serum samples: Whole blood will be withdrawn from each participant and then centrifuged to take the blood serum for testing (3-5 cc). *C*- Identification of the bacteria: A variety of aerobic and non-aerobic media will be inoculated with the swab, including 5% sheep blood agar, MacConkey agar, Mannitol salt agar, and chocolate agar, in the conventional manner. The distal part of the cut swab will be used to inoculate the plates during the swab processing procedure. The cultures will be cultured with 5% CO2 for an entire night at 37 °C. After an overnight incubation period, if there is no growth, the culture will be re-incubated for a full 24 hours. We will evaluate the bacterial growth using accepted methods.

D-Pure bacterial isolates will be identified at the species level by VITEK2 compact system. *E*-Total IgE tested by ELIZA serum analysis. *F*-Data Analysis: data will be introduced into specific software Statistical Package for the Social Sciences (SPSS) for statistical analysis.

C. Ethical approval

The study protocol will be forwarded to the appropriate ethics committee in the Karbala Health Directorate as well as the ethical committee at Karbala College of Medicine. Furthermore, before to collecting the sample, the patient's family members will be asked for verbal consent. Safety and health precautions shall be followed during sampling.

D. Statistical Analysis

The Real Statistics Resource Pack software for Mac (Release 7.2) of the resource pack for Excel 2016 and the Statistical Package for the Social Sciences software, version 28.0 (IBM, SPSS, Chicago, Illinois, USA), were used to verify, manage, and analyze all of the study group's data. (2013–2020) Copyright. The mean, standard deviation, frequencies, and percentages were displayed in descriptive statistics based on the categories of variables. Using the $\chi 2$-test and the T test to compare between groups, the data distribution was examined. Furthermore, to compare more than two groups, we employed the ANOVA test.

Moreover, post hoc analyses using multiple pairwise comparisons and least significant difference (LSD) were used to compare each of the two groups. In order to evaluate the efficacy of IL-37 and IL-38 in separating disease from the control group and establishing the cutoff point, receiver operating characteristic curve analysis (ROC) was employed.

Analytical statistical studies indicated significant variations in categorical variables among the parameters. All hypothesis test results with p-values less than 0.05 were deemed

statistically significant.

3. Result

One hundred participants were approached and consented to participate in this study from August 2023 to January 2024 patient (50%) and 50 control; had an Age Group ≤ 5 (interquartile range Less & equal than 3 in percent (41.0%), Greater than 3 in percent (60.0%). Baseline characteristics of the studied groups are shown in (Table 1), In the current study There were no- significant differences according to the age and sex when compared between the studied groups, (p-value 0.683) (p-value 0.343).

However, according to the Resident showed patient life in rural more connected with asthma and\or recurrent wheezer than urban ($p < 0.005$) due to life style and they relation with house animal, dust, smoke and insect. also, according to bacterial culturing there were highly significant differences ($p < 0.008$) when compared among patient's groups and with control group, where showed the S.Pneumonia, S.aureus most trending in patient group although these bacteria have virulence

Table 1
Distribution and characteristics of patients and control according to the study subjects

Variable	Level		Control	Patient	Total	P-Value
			Number (Percentage) %	Number (Percentage) %	Number (Percentage) %	
Age Group ≤ 5	Less & equal than 3		21 (42.0) %	19 (38.0) %	40(40.0)%	0.683
	Greater than 3		29 (58.0) %	31 (62.0) %	60(60.0)%	
Sex	Female		29 (58.0) %	23 (46.0)%	52(52.0)%	0.343
	Male		21 (42.0) %	27 (54.0)%	48(48.0)%	
Resident	Urban		32 (64.0)%	18 (36.0)%	50(50.0)%	0.005*
	Rural		18 (36.0) %	32 (64.0)%	50(50.0)%	
Bacteria	C.dephtheria		1 (2.0) %	1 (2.0)%	2(2.0)%	0.008*
	S.Mutans		7 (14.0)%	0 (0.0)%	7(7.0)%	
	S.Pneumonia		0 (0.0) %	11 (22.0)%	11(11.0)%	
	S.Saprophyticus		13 (26.0)%	0 (0.0)%	13(13.0)%	
	S.Xylose		0 (0.0)%	1 (2.0)%	1(1.0)%	
	H.influenza		5 (10.0) %	6 (12.0)%	11(11.0)%	
	K.Rosia		2 (4.0)%	5 (10.0)%	7(7.0)%	
	M.catarrhales		0 (0.0)%	5 (10.0)%	5(5.0)%	
	P.aerogenosa		0 (0.0)%	1 (2.0)%	1(1.0)%	
	S. Pyogen		10 (20.0)%	3 (6.0)%	13(13.0)%	
	S. aureus		3 (6.0)%	12(24.0)%	15(15.0)%	
	S. Epidermidis		9 (18.0)%	4 (8.0)%	13(13.0)%	
	S.Lentus		0 (0.0)%	1 (2.0)%	1(1.0)%	
Severity	None		50 (100.0)%	0 (0.0)%	50(50.0)%	0.002*
	Mild		0 (0.0)%	15(30.0)%	15(15.0)%	
	Moderate		0 (0.0)%	23 (46.0)%	23(23.0)%	
	Severe		0 (0.0)%	12 (24.0)%	12(12.0)%	
Treatment	None		50 (100.0)%	0 (0.0)%	50(50.0)%	0.002*
	Montelukast		0 (0.0)%	14 (28.0)%	14(14.0)%	
	ICS		0 (0.0)%	7 (14.0)%	7(7.0)%	
	ICS, Montelukast		0 (0.0)%	29 (58.0)%	29(29.0)%	
Response (Control)	None		50 (100.0)%	0 (0.0)%	50(50.0)%	0.001*
	Well		0 (0.0)%	19 (38.0)%	19(19.0)%	
	Not Well		0 (0.0)%	22 (44.0)%	22(22.0)%	
	Poorly		0 (0.0)%	8 (16.0)%	8(8.0)%	
	Severe		0 (0.0)%	1 (2.0)%	1(1.0)%	
Season	August	summer	0 (0.0)%	2 (4.0)%	2(2.0)%	0.003*
	September		0 (0.0)%	4 (8.0)%	4(4.0)%	
	October	autumn	2 (4.0)%	10 (4.0)%	12(12.0)%	
	November		3 (6.00%	27 (54.0)%	30(30.0)%	
	December	winter	17 (34.0)%	10 (20)%	27(27.0)%	
	January		28 (56.0)%	5 (10.0)%	33(33.0)%	
Eczema	Yes		0 (0.0)%	31 (62.0)%	31(31.0)%	0.002*
	No		50 (100.0)%	19 (38.0)%	69(69.0)%	
Allergic rhinitis/ conjunctivitis	Yes		0 (0.0)%	45 (90.0)%	45(45.0)%	0.001*
	No		50 (100.0)%	5 (10.0)%	55(55.0)%	
allergy Drug\ food	None		50 (100.0)%	25 (50.0)%	75(75.0)%	0.006*
	Penicillin		0 (0.0)%	14 (28.0)%	14(14.0)%	
	Spiecy		0 (0.0)%	11 (22.0)%	11(11.0)%	
History of asthma	Yes		0 (0.0)%	32 (64.0)%	32(32.0)%	0.001*
	No		50 (100.0)%	18 (36.0)%	68(68.0)%	
Animal in house	Yes		0 (0.0)%	32 (64.0)%	32(32.0)%	0.001*
	No		50 (100.0)%	18 (36.0)%	68(68.0)%	
Passive smoking	Yes		0 (0.0)%	36 (72.0)%	36(36.0)%	0.006*
	No		50 (100.0)%	14 (28.0)%	64(64.0)%	
	No		50 (100.0)%	0 (0.0)%	50(50.0)%	

The chi-square test has been utilized to analyze the categorical variables
*Association is significant at the 0.05 level

factor to influence on pathogenesis of asthma and increasing of exacerbation of symptoms, while in control showed S.Saprophyticus, S. Pyogen, S.Epidermidis was higher more than other species .In relation to the asthma severity of asthmatic patients, the results of study showed that there were highly significant differences between the patients group and control group where moderate type was dominant (46.0%) between three type of severity of disease. also, the results of this study showed that there highly significant differences in relation to treatment for the patient's groups with ICS, Montelukast where showed decreased and retard the symptoms. According to the Response (Control) by treatment (ICS, Montelukast) showed highly significant differences (p value-0.001) between studied group, there were 22(44.0)% not well, 19(38.0)% well, 8(16.0)% poorly,1 (2.0)% severe.

However, according to the Season, this study discovered highly significant connection between season and pediatric asthma and\or recurrent wheezer (p-value 0.003) so more patient was appearing in duration between autumn and winter that because more individual become exacerbation but lesser in summer.

More significant showed with patient have Eczema (p-value 0.002) where more individual (62.0)% have Eczema. Also individual with Allergic rhinitis/ conjunctivitis have highly significant (p-value 0.001) where (90.0)% of individual have Allergic rhinitis/ conjunctivitis. the results of this study showed that there highly significant differences (p-value 0.006) in relation to allergy Drug\food for the patient's groups with Penicillin, Spiecy. Family history of asthma was significantly more frequent in patients with pediatric asthma (P. value = 0.001) where (64.0)% of child they gained asthma of family, these mean the pediatric can inherited from parents. Animal in house have dominant role in relationship with asthma, so approximately) 64.0)% of individual that have cats, dogs, birds, became more exacerbation with asthma, significant differences (p-value 0.001). as for Passive smoking have highly significant (p-value 0.006), where (72.0)% of individual they gained Passive smoking by another people. (Table 1)

A statistically significant difference was found for the overall microbiome composition between asthmatic and control children (p=<0.001). The most common combination of organisms in asthmatics was Staphylococcus aureus and Streptococcus pneumoniae, and was statistically higher than in controls (0.01<0.001 respectively). Normal controls had a higher incidence of presence of coagulase negative staphylococci (*S. epidermidis S. saprophyticu* ,71.4%, 100.0% respectively) than the asthmatic group (28.6%, 0.0%). Kocuria rosea, although present more in asthmatics, the difference did not reach statistical significance. However, within the asthmatic group, the presence of K. rosea was noted more in patients with more severe asthma (p=0.26). (Table 2)

Of the total 100 patients of asthma, 15 (30.0%) mild persistent, 23 (46.0%) moderate persistent and 12 (24.0%) severe persistent asthma. The most frequent pathogen isolated from all pediatric groups was S. aureus (12 isolates) with predominance in modrate type of asthma severity, although these isolates have a higher number between them but no-significant relation with severity of asthma (p-value 0.33). followed by *S. pneumonia* (11 isolates) with predominance in moderate type of asthma severity, these isolates have significant relation to severity of asthma (0.021) followed by, *Haemophilus influenza* (6 isolates) with predominance in mild type of asthma severity. So, these isolates have significant relation with types of severity (<0.001). *K. rosia* was the fourth microorganism isolated (5 isolates) in this study with predominant in severe type of asthma severity, also these isolates have significant relation with types of severity (<0.001). *Moraxella* (5 isolates) found in all types of asthma severity, so these isolates have no-significant relation with types of severity (p-value 0.66).

Table 2
Relationship of bacterial growth with studying group

Bacteria		Patient	Control	Total	P-value
Corynebacterium	No.	1	1		1.00
	%	50.0%	50.0%	100.0%	ns
Haemophilus	No.	6	5	11	0.76
	%	54.5%	45.5%	100.0%	ns
K. rosia	No.	5	2	7	0.26
	%	71.4%	28.6%	100.0%	ns
Moraxella	No.	5	0	5	0.02*
	%	100.0%	0.0%	100.0%	sig
Pseudomonas	No.	1	0	1	0.49
	%	100.0%	0.0%	100.0%	ns
S. aureus	No.	12	3	15	0.01*
	%	80.0%	20.0%	100.0%	sig
S. epidermidis	No.	4	10	14	0.14
	%	28.6%	71.4%	100.0%	ns
S. lentus	No.	1	0	1	0.49
	%	100.0%	0.0%	100.0%	ns
S. mutans	No.	0	7	7	0.01*
	%	0.0%	100.0%	100.0%	sig
S. pneumonia	No.	11	0	11	<0.001*
	%	100.0%	0.0%	100.0%	sig
S. pyogens	No.	3	10	13	0.07
	%	23.1%	76.9%	100.0%	ns
S. saprophyticu	No.	0	13	13	<0.001*
	%	0.0%	100.0%	100.0%	sig
S. xylose	No.	1	0	1	0.49
	%	100.0%	0.0%	100.0%	ns
Total	No.	50	51	101	<0.001
	%	49.5%	50.5%	100.0%	

Chi square test
*Association is significant at the 0.05 level

S. epidermidis (4 isolates) with predominance in mild and moderate type of asthma severity but in less count, so these isolates have no- significant relation with types of severity (0.41). *S. pyogen* (3 isolates) with predominance in mild type of asthma severity, so these isolates have significant relation with types of severity (p-value 0.02). *On the other hand, Corynebacterium, Pseudomonas, S. lentu, S. xylose,* least isolated in pediatric pathogen were isolated from pediatric group (1,1,1,1 respectively isolate) so all these isolates have no-significant relation with types of severity (p- value 0.30, 0.39, 0.39, 0.39 respectively).

Based on morphological and VITEK compact system results, the culture research revealed that the patient group has a rate of 50(100%), with S. aureus showing the highest proportion at 12(24.00)%, followed by S. pneumoniae at 11(22.00)%. Next

Table 3
Bacterial species among asthma severity class in patient group

Bacteria		Severity			Total	P- value
		Mild	Moderate	Severe		
Corynebacterium	No.	1	0	0	1	0.30
	%	100.0%	0.0%	0.0%	100.0%	
Haemophilus.	No.	5	1	0	6	<0.001*
	%	83.3%	16.7%	0.0%	100.0%	
K. rosia	No.	0	0	5	5	<0.001*
	%	0.0%	0.0%	100.0%	100.0%	
Moraxella	No.	1	2	2	5	0.66
	%	20.0%	40.0%	40.0%	100.0%	
Pseudomonas	No.	0	1	0	1	0.39
	%	0.0%	100.0%	0.0%	100.0%	
S. aureus	No.	2	8	2	12	0.33
	%	16.7%	66.7%	16.7%	100.0%	
S. epidermidis	No.	2	2	0	4	0.41
	%	50.0%	50.0%	0.0%	100.0%	
S. lentus	No.	0	1	0	1	0.39
	%	0.0%	100.0%	0.0%	100.0%	
S. pneumonia	No.	1	7	3	11	0.021*
	%	9.1%	63.6%	27.3%	100.0%	
S. pyogen	No.	3	0	0	3	0.02*
	%	100.0%	0.0%	0.0%	100.0%	
S. xylose	No.	0	1	0	1	0.39
	%	0.0%	100.0%	0.0%	100.0%	
Total	No.	15	23	12	50	<0.001
	%	30.0%	46.0%	24.0%	100.0%	

Chi square test
*Association is significant at the 0.05 level

in order of percentage are H. influenza 6 (12.00)%, K. rosia 6 (12.00)%, M.catarrhales 5 (10.00)%, and S. epidermidis 4 (8.00)%. S. xylose 1(2.00) % and Pseudomonas 1(2.00) % are the final two. S. pyogen 3(6.00) %. In contrast, the control group recorded 50(100%), of which the majority of isolated bacteria in this study, S. saprophyticus, made up percentages of 12(25.50)%, S. pyogen 10(19.60)%, S. mutans 7(13.70)%, H.influenza 5(9.80)%, S. aureus 3(5.90)%, K. rosia 2(3.90)%, and Corynebacterium 1(2.00)%, as indicated in (figure1 and 2).

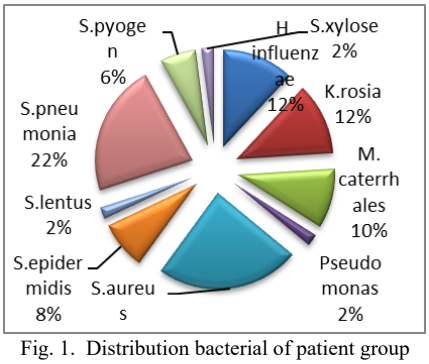

Fig. 1. Distribution bacterial of patient group

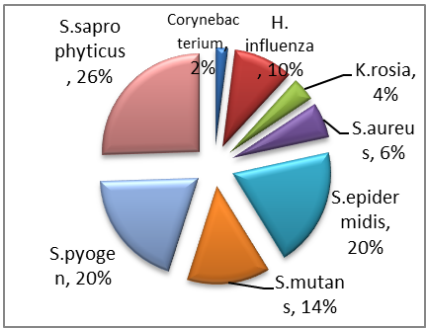

Fig. 2. Distribution bacterial of control group

4. Discussion

Our finding showed that nasopharyngeal microbiome spectrum of composition was found to be different among those with asthma and the control group (p= <0.001), and even among those K. rosea appeared in patient with severe asthma (p= <0.001). Our findings confirm the earlier reports of difference in microbiome composition among exacerbated. asthma, non-exacerbated asthma, and healthy child.

All patient with asthma or recurrent wheezer has high total IgE levels (>60 UI/mL), presented a higher abundance of Firmicutes (Staphylococcus, Streptococcus) and lower of Proteobacteria (Moraxella, Haemophilus, Neisseria)

In our study, we excluded the children who received antibiotics in the last two weeks before sampling which is usually enough to reverse the effect on the nasopharyngeal microbiome, VITEK uses a known nutrients and biochemical reactions of the microorganism to make the identification. This necessitates a sufficient amount of growth in a growth culture over a period of 18 – 70 hours.

According to the World Health Organization (WHO), probiotics are live microorganisms that are good for the host and have the ability to colonize the body and change the makeup of the flora in particular areas. Research on their possible advantages in managing and preventing asthma is still ongoing [16]. The type and quantity of the microbiome in the lungs can be influenced by a number of internal and external factors, including age, nutrition, lifestyle, genetics, cigarette smoke, pollution exposure, and possible diseases. These factors may result in dysbiosis of the respiratory flora. In response to inflammatory reactions and immunological modulation linked to host asthma, the respiratory microbiome plays an important role in regulating immunity, cellular function, and metabolism.

It could modify asthma phenotypes, affect asthma severity, and mediate host susceptibility to asthma [17]. Asthma risk is increased in infancy by disruptions in the microbiota and metabolic abnormalities, and these effects may continue throughout preschool. Asthma development and chronicity are largely dependent on the microbiome's temporal and dynamic interactions with immunity, which play a critical role in modifying immune function [18]. According to one study, children with asthma had a considerably different nasopharyngeal microbiome composition than their peers in good health. While the combination of Staph. aureus and Strep. pneumoniae was higher in asthmatic patients, COAGULASE negative staphylococci (CONS) were considerably higher in healthy controls. It was discovered that children with more severe asthma and younger asthmatics were more likely to have Kocuria rosea [19]. Early life acquisition of S. aureus is frequently linked to high nasal colonization, which is estimated to be as high as 30% in the general population [20]. When Clostridium difficile colonized a baby at one month old, it was linked to asthma at six or seven years old and wheezing for the next six or seven years. [21].

Elevated blood levels of eosinophil IgE and a higher incidence of asthma and wheeze at age five are linked to upper respiratory colonization with pneumococcus and Haemophilus influenza at 4 weeks of age [22].

In one such study, nasal microbiological samples showed that when the Corynebacterium Dolosigranulum flora switched to Moraxella in the early phases of uncontrolled asthma, there was a predicted higher chance of inflammatory asthma getting worse [23]. The gut-lung axis is probably crucial for preserving a healthy microbiome in the lungs and gut, affecting both systems' immune responses, and preserving homeostasis in vivo [24]. Dysbiosis in gut and lungs appears as a key contributor to the increased prevalence of asthma [25]. The gut microbial makeup during the first year of life was associated with a later risk of asthma, according to a study by J. Stokholm et al. [26].

Limitation of our study: There is a dearth of information on the nasopharyngeal microbiota during severe exacerbations and little distinction between the severity levels of exacerbations. In order to gain a deeper understanding of the composition of the nasopharyngeal microbiome and its role in severe asthma, we first looked into the differences in the nasopharyngeal microbiota between children who were experiencing an asthma exacerbation and children who were healthy controls. The secondary goals were to investigate the factors influencing upper airway microbial populations that were related to the patient (administration of inhaled corticosteroid [ICS]), as well as the environment (passive smoking, having an animal in the house, history of asthma, allergic rhinitis, and season).

A. Recommendation

- Anybody who is sensitized to an allergen should identify them and implement a systematic approach to either remove or significantly reduce them.
- Clinicians ought to advocate for suitable environmental management for patients who exhibit sensitivities to household dust mites.
- Medical practitioners ought to keep advising against being around tobacco smoke.
- Physicians should identify allergens to which any person is sensitized and develop a systematic program to eliminate or significantly reduce them. The many additional advantages of breastfeeding make it a recommended practice.

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