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Cortisol Level in Patients Presenting with Asthma Exacerbation

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ABSTRACT

Background: Asthma is a chronic inflammatory airway disease characterized by recurrent episodes of wheeze, cough, chest tightness, and shortness of breath. **Objective:** To compare salivary cortisol levels in patients with and without acute exacerbation of asthma. **Methodology:** This cross-sectional study was conducted at the Central Park teaching hospital, Lahore, from 15 March 2025 to 15 June 2025. A total of 100 patients aged 16–60 years with diagnosed asthma were enrolled through non-probability consecutive sampling. Patients with bleeding diathesis, severe dyspnea, pulmonary or extrapulmonary tuberculosis, pleural effusion, or malignancy were excluded. Demographic and clinical information was recorded on a structured proforma. **Results:** The mean age of the patients was 34.82 ± 11.46 years, mean body mass index was 25.91 ± 4.28 kg/m^2, and mean duration of asthma was 6.74 ± 3.81 years. There were 58 (58.0%) males and 42 (42.0%) females. Acute exacerbation of asthma was present in 36 (36.0%) patients and absent in 64 (64.0%). The mean salivary cortisol level in patients with acute exacerbation was significantly lower than in those without exacerbation (6.71 ± 2.18 ng/mL vs 9.71 ± 2.77 ng/mL, p<0.001). Acute exacerbation was also significantly more frequent among patients with anemia, smoking history, and asthma duration greater than 5 years. **Conclusion:** It is concluded that patients presenting with acute exacerbation of asthma had significantly lower salivary cortisol levels than patients without exacerbation.

INTRODUCTION

Nevertheless, patients with asthma have exacerbations, which are triggered by an increase in the severity of underlying diseases and a loss of control over the disease [1]. Among the most frequent causes of disease morbidity, rises in health care costs and in some patients, a progressive more severe loss of lung function are asthma exacerbations [2,3]. The serious asthma attack may be a terrifying experience to the patient and doctor. Even though the management rules and progress in treatment continue to be made, severe exacerbations continue to take place. To anticipate and prudent control of asthma attacks, we must forecast them first [4]. Asthma is a very common chronic respiratory illness with 300 million individuals in the world infected with asthma. A large proportion of the cost and morbidity of asthma is associated with acute care of asthma attacks [5,6]. Adrenal functioning in the stable asthmatic patient, asthmatic patient undergoing high dose corticosteroid therapy and asthmatic patient admitted to the hospital due to life threatening exacerbation have been widely studied. The idea that asthmatic patients in a stable condition have a dysfunctional hypothalamic-pituitary-adrenal axis and the notion that acute exacerbation is, in part, caused by inadequate endogenous production of corticosteroids has long been dismissed [7]. In one study, which was conducted in Korea, it was reported that among all the patients affected by asthma, 34.5% of them would present with acute exacerbation of asthma. The average level of cortisol was 0.14±0.08 µg/dl in patients with acute exacerbation of asthma that was significantly lower than that of patients with controlled asthma (0.18±0.11 µg/dl) [8]. The connection that exists between asthma and cortisol, however, is not entirely clear. Other studies have proposed that acute severe asthma is linked to elevation in plasma cortisol concentrations, which is a reflection of activation of the stress response. An example is a pediatric study that reported that the plasma cortisol levels of children with severe acute asthma were significantly higher than those with moderate attacks [9]. Conversely, a previous study of acute asthma in the emergency department concluded that most exacerbations did not result in a strong physiologic stressor response and that only a few patients were adrenally suppressed on presentation [10]. This discrepancy implies that the level of cortisol during asthma exacerbation can be inconsistent depending on the severity of the attack, prolonged

exposure to chronic steroids, the time of the sample and the responsiveness of individual adrenal. This is a clinical issue since a lot of asthmatics are exposed to inhaled or systemic corticosteroids, which can both influence endogenous cortisol secretion [11]. Meta-analytic and review evidence has demonstrated that inhaled corticosteroids have the ability to suppress the production of adrenal cortisol, particularly at higher dosages or with the prolonged use [12]. Consequently, the cortisol concentration in patients who present with the exacerbation of asthma may reflect the result of a mixture of acute physiologic stress, underlying disease activity, and the hypothalamic-pituitary-adrenal axis suppression due to treatment. That makes cortisol potentially helpful not only as a level of hormone, but as a biomarker associated with severity, chronic exposure to steroids, and adrenal reserve [13].

Objectives

- To assess the frequency of patients presenting with acute exacerbation of asthma
- To compare the mean cortisol level in patients presenting with and without acute exacerbation of asthma.

METHODOLOGY

This cross-sectional study was conducted at the Central Park teaching hospital, Lahore, From 15 March 2025 to 15 June 2025. Using the WHO sample size calculator, a sample size of 100 cases was calculated at a 95% confidence level, a 9.5% margin of error, and an acute exacerbation of asthma prevalence of 34.5% in asthmatic patients. Non-probability consecutive sampling was used to collect the data. The respondents were patients of both genders aged 1660 years with diagnosed asthma as per the operational definition. Patients who had a bleeding diathesis or a severe dyspnea were not eligible. Those patients with pulmonary or extrapulmonary tuberculosis, pleural effusion, or malignancy recorded on a medical record were also excluded.

Data Collection

One-hundred patients meeting the selection criteria were recruited at the outpatient department. All the participants were informed and provided informed written consent. Demographic and clinical data such as name, age, sex, body mass index, duration of asthma, residence, socioeconomic status, number of relatives, occupation, history of diabetes mellitus, hypertension, anemia, smoking, alcoholism, family history of asthma and treatment under-taken to treat asthma were taken. Diabetes was taken into consideration when blood sugar random exceeded 200 mg/dL, hypertension when blood pressure was above 140/90 mmHg, anemia where blood hemoglobin was less than 10 g/dL, smoking when history had over 5 pack years, alcoholism when intake exceeded 20 mL/day. All the patients were studied based on the presence or absence of acute exacerbation of asthma according to the operational definition and divided into two groups respectively. Salivary samples were then taken with the help of cotton swabs. All samples were placed in the hospital laboratory where cortisol level was assessed. The review and the recording of cortisol levels were made according to operational definition. All the details were recorded on a structured proforma.

Data Analysis

Data was fed and processed in SPSS version 25. The ShapiroWilk test was used to test the normality of data. Continuous variables like age, body mass index, asthma duration, and cortisol level were measured using mean and standard deviation. The categorical variables, such as gender, residence, socioeconomic status, number of family members, occupation, diabetes, hypertension, anemia, smoking, alcoholism, family history of asthma, asthma treatment, and acute asthma exacerbation were calculated using frequency and percentage. the independent-samples t-test was used to compare the mean cortisol level between patients with and without the acute asthma exacerbation. A p-value of ≤0.05 was taken as statistically significant. Data were stratified for age, gender, residence, socioeconomic status, number of family members, occupation, diabetes, hypertension, anemia, smoking, alcoholism, family history of asthma, treatment of asthma, body mass index, and duration of asthma. The frequency of acute exacerbation of asthma was compared using stratified groups in chi-square test, and mean cortisol level was compared between patients with and without acute exacerbation within each stratum using independent samples t -test. A p-value of ≤0.05 was considered significant.

RESULTS

Data were collected from 100 patients, mean age of the participants was 34.82 ± 11.46 years, the mean body mass index was 25.91 ± 4.28 kg/m^2, and the mean duration of asthma was 6.74 ± 3.81 years. Males constituted 58 (58.0%) of the study population, while females accounted for 42 (42.0%). Most patients belonged to urban areas, 61 (61.0%), compared with 39 (39.0%) from rural areas. Regarding socioeconomic status, 43 (43.0%) patients belonged to the middle socioeconomic group, 37 (37.0%) to the low group, and 20 (20.0%) to the high group.

Table 1

Baseline characteristics of study participants (n=100)

Variable	Category	n (%) / Mean ± SD
Age (years)	Mean ± SD	34.82 ± 11.46
BMI (kg/m^2)	Mean ± SD	25.91 ± 4.28
Duration of asthma (years)	Mean ± SD	6.74 ± 3.81
Gender	Male	58 (58.0%)
	Female	42 (42.0%)
Residence	Urban	61 (61.0%)
	Rural	39 (39.0%)
Socioeconomic status	Low	37 (37.0%)
	Middle	43 (43.0%)
	High	20 (20.0%)
Family members	≤5	46 (46.0%)
	>5	54 (54.0%)
Occupation	Employed	41 (41.0%)
	Unemployed/household	59 (59.0%)

Among the clinical characteristics, diabetes mellitus was present in 14 (14.0%) patients, hypertension in 19 (19.0%), anemia in 17 (17.0%), smoking in 21 (21.0%),

and alcoholism in 8 (8.0%) patients. A family history of asthma was noted in 29 (29.0%) patients, whereas 71 (71.0%) had no such history. Most patients, 72 (72.0%), were receiving inhaled treatment for asthma, while 28 (28.0%) were on oral or irregular treatment.

Table 2
Clinical characteristics of study participants (n=100)

Variable	Category	n (%)
Diabetes mellitus	Yes	14 (14.0%)
	No	86 (86.0%)
Hypertension	Yes	19 (19.0%)
	No	81 (81.0%)
Anemia	Yes	17 (17.0%)
	No	83 (83.0%)
Smoking	Yes	21 (21.0%)
	No	79 (79.0%)
Alcoholism	Yes	8 (8.0%)
	No	92 (92.0%)
Family history of asthma	Yes	29 (29.0%)
	No	71 (71.0%)
Treatment of asthma	Inhaled treatment	72 (72.0%)
	Oral/irregular treatment	28 (28.0%)
Acute exacerbation of asthma	Present	36 (36.0%)
	Absent	64 (64.0%)

Patients with acute exacerbation had a mean cortisol level of 6.71 ± 2.18 ng/mL, while those without exacerbation had a mean cortisol level of 9.71 ± 2.77 ng/mL. This difference was highly statistically significant ($p < 0.001$).

Table 3
Comparison of salivary cortisol level in patients with and without acute exacerbation of asthma

Variable	Acute exacerbation present (n=36)	Acute exacerbation absent (n=64)	p-value
Cortisol level (ng/mL), Mean ± SD	6.71 ± 2.18	9.71 ± 2.77	<0.001

On stratification analysis, the frequency of acute exacerbation was higher in females (40.5%) than males (32.8%), although this difference was not statistically significant ($p = 0.451$). Similarly, exacerbation was slightly more common among urban residents (39.3%) than rural residents (30.8%), but this difference was also not significant ($p = 0.426$). In contrast, significant associations were observed with anemia, smoking, and duration of asthma. Among anemic patients, 64.7% had acute exacerbation compared with only 30.1% of non-anemic patients ($p = 0.008$).

Table 4
Stratification of acute exacerbation by selected variables

Variable	Category	Acute exacerbation present n (%)	Acute exacerbation absent n (%)	p-value
Gender	Male	19 (32.8%)	39 (67.2%)	0.451
	Female	17 (40.5%)	25 (59.5%)	
Residence	Urban	24 (39.3%)	37 (60.7%)	0.426
	Rural	12 (30.8%)	27 (69.2%)	
Anemia	Yes	11 (64.7%)	6 (35.3%)	0.008
	No	25 (30.1%)	58 (69.9%)	
Smoking	Yes	13 (61.9%)	8 (38.1%)	0.011
	No	23 (29.1%)	56 (70.9%)	
Duration of asthma	≤5 years	12 (23.1%)	40 (76.9%)	0.006
	>5 years	24 (50.0%)	24 (50.0%)	

Among males, the mean cortisol level was 6.94 ± 2.31 ng/mL in patients with exacerbation compared with 9.83 ± 2.66 ng/mL in those without exacerbation ($p < 0.001$). Among females, the corresponding values were 6.46 ± 2.05 ng/mL and 9.52 ± 2.98 ng/mL, respectively ($p = 0.002$). In anemic patients, cortisol levels were 5.98 ± 1.82 ng/mL in those with exacerbation versus 8.14 ± 2.11 ng/mL in those without exacerbation ($p = 0.031$). Among smokers, the mean cortisol level was 6.12 ± 2.07 ng/mL in the exacerbation group compared with 8.76 ± 2.25 ng/mL in the non-exacerbation group ($p = 0.018$).

Table 5
Stratified comparison of salivary cortisol level according to exacerbation status

Strata	Acute exacerbation present Mean ± SD	Acute exacerbation absent Mean ± SD	p-value
Male	6.94 ± 2.31	9.83 ± 2.66	<0.001
Female	6.46 ± 2.05	9.52 ± 2.98	0.002
Anemia present	5.98 ± 1.82	8.14 ± 2.11	0.031
Smoking present	6.12 ± 2.07	8.76 ± 2.25	0.018
Duration of asthma >5 years	6.55 ± 2.14	9.21 ± 2.61	<0.001

DISCUSSION

The current study was conducted to determine the levels of salivary cortisol in patients who present with asthma and compares with patients who present with acute exacerbation. The key study results were that the mean levels of salivary cortisol were significantly lower in patients with acute exacerbation of asthma in comparison to patients who did not experience acute exacerbation of asthma. This implies that the decreased response to endogenous cortisol may be related to acute asthma worsening and may have a role in the pathophysiology or severity of exacerbation. A total of 100 patients were included in the study, with a mean age of 34.82 ± 11.46 years and a mean body mass index of 25.91 ± 4.28 kg/m^2. Males were predominantly more than females and a majority of the participants were urban dwellers. In 36.0 percent of patients, there was acute exacerbation. This rate is in line with the clinical burden of asthma exacerbation observed in outpatient and inpatient environments, where an appreciable number of known asthmatic patients present with acute symptom worsening despite ongoing therapy [14].

The most significant finding of this study was the significant difference between the level of cortisol between the two groups. The average level of salivary cortisol in patients with acute exacerbation was 6.71 ± 2.18 ng/mL, as opposed to 9.71 ± 2.77 ng/mL in the patients with no exacerbation, and the difference was highly significant. The body has a significant endogenous glucocorticoid, cortisol, which is likely to be involved in the regulation of inflammation during physiologic stress. As exacerbations of asthma are acute inflammatory events, the lower cortisol levels in the exacerbation group may indicate an inadequate adrenal response or relative suppression of the hypothalamic-pituitary-adrenal axis [15]. This observation confirms the fact that a

compromised endogenous corticosteroid activity could be the cause of ineffective inflammatory control in the case of acute asthma attacks. One more pertinent result was that exacerbation was more common with some clinical subgroups. Asthma patients with a history of anemia, smoking, and longer asthma duration had much higher rates of acute exacerbation. In anemic patients, acute exacerbation was also found to be significantly high in smokers as well. Likewise, patients who had a duration of asthma that was longer than 5 years had significantly more exacerbations compared to other patient groups [16]. These results indicate that chronic disease burden, physiological stress, and modifiable risk factors like smoking can contribute to asthma control and predispose patients to acute attacks. The stratified comparison of cortisol levels served to further reinforce the main finding of the study. The amount of cortisol in exacerbation group and non-exacerbation group in both sexes was significantly lower in exacerbation group as compared to non-exacerbation group in both sexes [17-19]. The same trend was noted in patients with anemia, smokers, and those with asthma duration more than 5 years. This uniformity in the relationship between low cortisol and acute exacerbation is significant in that it implies that the relationship between low cortisol and acute exacerbation is not exclusive to only one subgroup. Instead, it seems to be a more general and stable clinical pattern [20]. There are certain limitations of this study. It was carried out at one center and with a relatively small sample size which could restrict the generalizability of the results. The cross-sectional design is unable to cause inference and this design cannot be stated to directly cause exacerbation or merely it accompanies exacerbation. Moreover, the measurement of cortisol was done on one salivary sample, no serial measurements were done. Data on definite dose and duration of corticosteroid therapy might also affect cortisol levels and was not studied in more depth. Nonetheless, despite these shortcomings, the study nonetheless presents valuable evidence that salivary cortisol significantly varies with exacerbation status in asthmatic patients.

CONCLUSION

It is concluded that patients presenting with acute exacerbation of asthma had significantly lower salivary cortisol levels than patients without exacerbation. Acute exacerbation was also found to be more frequent among smokers, anemic patients, and those with longer duration of asthma. These findings suggest that reduced cortisol level may be associated with acute asthma exacerbation and may reflect an inadequate endogenous anti-inflammatory response during disease worsening.

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