University of Thi-Qar Journal of Science (UTJsci)
E-ISSN: 2709-0256, P-ISSN: 1991-8690, Vol. 11, No. 2, Dec. 2024

The Relationship Between Iron Deficiency and Asthma Severity: Detection The Role of Gender and Ferritin Level

Samih Riyadh Faisal

Al-Manara College for Medical Sciences, Maysan, Iraq

E-mail: Samih2.riyadh2@gmail.com

Received: 2024-06-09, Revised: 2024-07-06, Accepted: 2024-07-18, Published: 2024-12-05

Abstract*— Emerging research suggests a complex interplay between asthma severity and ferritin levels, with evidence indicating that lower serum ferritin may be associated with increased asthma exacerbations, highlighting the potential role of iron homeostasis in respiratory health and disease management. The study aims to examine the impact of ferritin levels on asthma severity, assess the moderating effect of gender, and identify biomarkers that exacerbate symptoms in the context of low ferritin. This study enrolled 180 individuals over 18 years, including 120 allergic asthma patients and 60 healthy controls. Asthma patients were categorized based on ferritin levels into 43 males and 17 females with normal levels, and 17 males and 43 females with low levels. The study excluded individuals with other respiratory, autoimmune, or oncologic diseases, and smokers. Blood samples were collected for complete blood count (CBC), ferritin, and Immunoglobulin E (IgE) measurements, with serum samples frozen at -70°C for further analysis. Out of 180 participants, 120 (66.6%) were asthma cases, split evenly between normal and low ferritin levels. The study found significant hematocrit differences ($P < 0.01$), with the lowest levels in the low ferritin asthma group (35.18 ± 6.74). Ferritin and IgE levels varied markedly across groups ($P < 0.05$ and $P < 0.001$, respectively), with the lowest ferritin (9.80 ± 2.39 ng/ml) and highest IgE (327.91 ± 106.81 IU/ml) in the low ferritin asthma group. Regression analysis showed an inverse relationship between ferritin levels and asthma severity ($B = -20.46$, $P < 0.001$), and moderation analysis indicated sex as a significant moderator ($P = 0.033$). This study reveals a significant link between anemia and allergic asthma severity, with gender differences influencing the relationship between ferritin and IgE levels. The results underscore the exacerbating effect of iron deficiency on asthma symptoms and the critical role of iron management in treatment protocols.

Keywords*— *Asthma, IgE, Ferritin, Moderation analysis, Hemoglobin, Hematocrit.

I. INTRODUCTION

Allergic asthma manifests as a chronic inflammatory disorder and represents the predominant phenotype of asthma. Characterized by hypersensitivity to environmental allergens, this condition precipitates constriction of the bronchial passages. Globally, asthma afflicts approximately 300 million individuals [1]. A plethora of research endeavors have been dedicated to elucidating risk factors associated with asthma. A recurrent finding is the familial aggregation of asthma indicating a substantial genetic contribution to the etiology of the disease [2,3]. Additionally, factors intrinsic to the individual and their environment, such as obesity [4], exposure to air pollutants, and inhalation of tobacco smoke, have been implicated in heightened asthma vulnerability. Asthma's pathophysiological mechanisms are known to perturb iron balance, potentially leading to anemic states. Nonetheless, the interplay between asthma and anemia in adult cohorts warrants further exploration [5,6]. The past decade has witnessed significant strides in deconstructing asthma's cellular and molecular underpinnings. Dysregulated T helper type 2 (Th2) immune responses emerge as a central pathological feature of asthma, orchestrated by Th2 cytokines like interleukin (IL)-5, IL-4, and IL-13. Notably, Th2-driven inflammation accounts for roughly half of mild-to-moderate asthma cases and a substantial fraction of severe instances. Conversely, Th2-low asthma phenotypes may arise from the influence of non-Th2 cytokines, such as IL-17 and tumor necrosis factor-α. Recent discoveries underscore the role of inflammation-independent pathways in asthma's progression, with protein kinases, adapter proteins, microRNAs, ORMDL3, and gasdermin B identified as key drivers of disease advancement, irrespective of inflammatory status. For Th2-high asthma, eosinophil, IgE, fractional exhaled nitric oxide, and periostin serve as utilitarian biomarkers. In contrast, sputum neutrophil counts facilitate the diagnosis of Th2-low asthma [7].

Ferritin, an iron sequestration molecule, mirrors the body's iron reserves in plasma or serum; reduced ferritin levels signal for iron deficiency, whereas augmented levels may indicate a propensity for iron overload. It is noteworthy that ferritin also functions as an acute-phase reactant, with concentrations rising amid inflammation and infection [8].

The regulation of iron is critically entwined with the pathogenesis of allergic asthma, where ferritin concentrations act as a indicator of iron status. The incidence of iron-deficiency anemia (IDA) is disproportionately elevated among asthmatic pediatric populations, hinting at a potential interconnection between iron bioavailability and respiratory functionality [9]. Hemoglobin concentrations, indicative of iron reserves, exhibit a positive correlation with pulmonary performance indicators, emphasizing the necessity of sufficient iron for optimal respiratory health [10]. Moreover,

https://doi.org/10.32792/utq/utjsci/v11i2.1269

females with ample iron stores experience reduced asthma manifestations, while a decline in circulating iron coupled with an uptick in tissue iron demand correlates with compromised lung function [11].

The immunological reaction to allergens is intimately linked with iron levels. Individuals with atopic predispositions, prone to allergic manifestations, typically display a Th2-skewed immune landscape [12]. Iron deficits can intensify this predisposition by fostering the proliferation of Th2 lymphocytes which is pivotal in eliciting allergic reactions. Furthermore, iron paucity can modulate B-cell isotype switching and M2 macrophage activation, both integral to the organism's allergenic response [13,14]. Certain allergens, especially those harboring lipocalin motifs, can hijack iron via siderophores, thereby contributing to allergic sensitization [15]. Cutting-edge research has also cast light on the significance of ferroptosis, an iron-centric cell death modality, in the context of asthma [15,16]. The induction of NCOA4-mediated ferritinophagy, a selective autophagic process triggered by allergens, intimates that modulating ferroptosis may present a novel therapeutic strategy for asthma precipitated by allergens [17]. This study aims to investigate how ferritin levels affect asthma severity by comparing the patients with low ferritin versus normal ferritin levels. It also explores how gender may work as a moderator in this relationship and identifies additional biomarkers that could intensify asthma symptoms when ferritin is low.

II. Materials and Methods

A. Study population

A total of 180 individuals aged more than 18 years were enrolled in the study. Of them, 120 patients had stable allergic asthma, which was untreated with any given doses of inhaled glucocorticoids for more than 3 months (diagnosed according to the Global Initiative for Asthma [18] recommendations). Samples were collected from January to June, 2024. With mentioned that none of the all participants took Iron supplementation before doing this study for at least one year. The exclusion criteria were as follows: None of the groups showed any acute and chronic respiratory diseases (except allergic asthma), pregnancy, autoimmune diseases or oncologic diseases were also excluded, and only non-smokers individuals were selected. Participants were recruited from (Misan City, Iraq), and only patients who lived in the urban were included. Oral informed consent was obtained from all individual participants included in the study. Participants were provided with a detailed explanation of the study's purpose, procedures, potential risks, and benefits. They were informed of their right to withdraw from the study at any time without any consequences.

B. Peripheral blood collection and processing

CBC, ferritin level, and serum total IgE were measured in peripheral blood. Peripheral blood was collected by peripheral venipuncture according to the standard procedure. Blood samples were drawn into K3 ETDA tubes for enumeration of CBC by Horiba ABX SAS Company (Montpellier, FR, USA), and serum tube stored at room temperature for 15-20 min and centrifuged for 10 min at 4000 rpm. Serum samples were instantly frozen at -70°C for more analysis.

C. Measuring of Ferritin level and IgE level

Concentration of ferritin level in serum was measured by HP-AFS/1 immunoassay Analyzer, while IgE level in serum was measured using the enzyme-linked immunosorbent assay ELISA (by kit (Bio-Clin, USA) according to the manufacturer's recommendations..

D. Statistical analysis

Statistical analysis was performed using the statistical program SPSS 24. Shapiro Wilk test was used to test the normality of distribution for data, and then methods of statistics were selected after making sure all the data was normally distributed. T- test was used to compare the difference between two groups, also one way ANOVA was used to compare between more than two groups, Chi-Square was used for categorical variables, Methods of correlation Pearson coefficient and multiple linear regression analysis were used in order to find associations between IgE levels Ferritin levels, Hemoglobin, Hematocrit, Age, and sex. Moderation analysis was used to assess a third variable on the relationship between the dependent and independent variables, the PROCESS macro in SPSS software was used for the analysis . A P-value of < 0.05 was considered statistically significant.

III. RESULTS

A. Characteristics of study population

Of 180 participants, 120 (66.6%) were assessed in the case group and 60 (33.3%) as a control group. Of the total case groups were divided into two subgroup 60 (50%) were asthma patients with normal ferritin level and 60 (50%) asthma patients with low ferritin level. In the asthma patients with normal ferritin, males were 43 (71%) while the rest 18 (29%) was females. Moving to asthma patients with low ferritin level subgroup, males were 17 (29%), whereas females recorded 43 (71%). And the control group, males was 33 (54.8%), although female was 27 (45.2%) (Table 1). The mean age (± standard deviation, in years) for subgroup asthmatic patients with normal ferritin levels was 33.7 ± 8.42, and 33.90 ± 11.01 for asthma patients with low ferritin levels, for the control group, the mean and SD was 35.77 ± 9.24 (Table 1).

B. Comparison of laboratory tests between the study groups

In the conducted study, as seen in (Table2.), the analysis of hematocrit values revealed a markedly significant differences among the groups. The control group exhibited a mean hematocrit of 42.37 (± 5.56) compared with the 44.57 (± 4.09) of the asthma group with normal ferritin levels, and was substantially higher than the 35.18 (± 6.74) noted in the asthma group with low ferritin levels, with the differences yielding a P-value less than 0.01.

Ferritin levels themselves were significantly different across the groups, with the control group averaging 121.37 (± 57.13), the asthma group with normal ferritin levels at 111.02 (± 38.74), and the asthma group with low ferritin

levels at a noticeably reduced 9.80 (± 2.39), as indicated by a P-value less than 0.5.

Table 1- Characteristics of the study population

Characteristics	Asthma group with normal ferritin levels (N=60)	Asthma group with low ferritin levels (N= 60)	Control group (N= 60)
Sex			
Male, n	43 (71%)	17 (29%)	33 (54.8%)
Female, n	17 (29%)	43 (71%)	27 (45.2%)
Age			
Male/Female,years	33.7 ± 8.42	33.90 ± 11.01	35.77 ± 9.24

Values are mean ± standard deviation of the mean

Lastly, IgE levels demonstrated a highly significant statistical difference, with the control group averaging 42.86 (± 17.46), the asthma group with normal ferritin levels significantly higher at 251.93 (± 96.39), and the asthma group with low ferritin levels further elevated at 327.91 (± 106.81), corroborated by a P-value less than 0.01.

Table 2. Estimation of hematological parameters, ferritin level, IgE level in studied groups

Variables	Asthma group with normal ferritin levels	Asthma group with low ferritin levels	Control group
Hemoglobin g/dl	12.64 ± 1.07	11.62 ± 3.41	12.45 ± 1.65
Hematocrit %	44.57 ± 4.09**	35.18 ± 6.74**	42.37 ± 5.56**
White Blood Cells count 10^3 /mm^3	6.87 ± 1.68	7.00 ± 1.66	6.56 ± 1.42
Ferritin ng/ml	111.02 ± 38.74*	9.80 ± 2.39*	121.37 ± 57.13*
Immunoglobulin E IU/ml	251.93 ± 96.39**	327.91 ± 106.81**	42.86 ± 17.46**

*P < 0.05
**P < 0.01

C. *Predictive factors in multiple regression analysis*

In the regression model presented in Table 3. The analysis identified two variables with notable statistical significance. The variable Ferritin demonstrated a substantial inverse effect on the dependent variable (asthma severity), with a B-coefficient of -20.46, r= - 0.65, 95% CI (-26.53 – -14.40) (P< 0.001), indicated that higher levels of ferritin are associated with a decrease in the asthma severity. Furthermore, the variable Age showed a positive relationship with the dependent variable, evidenced by B-coefficient 3.399, r= 0.30, 95% CI (0.31 – 6.48) (P= 0.031). This indicated that the dependent variable (asthma severity) tends to increase with age, which may reflect the cumulative effects of aging or the increased prevalence of risk factors over time.

Table 3. Coefficient and P- values of the independent variables in the multiple regression model

Variables	B-coefficient	Std. Error	95% CI	P-value	r
Constant	528,58	32.54	463.48 – 593.68	0.001	
Ferritin	-20.46	3.03	-26.53 – -14.40	0.001	- 0.65
Sex	49.169	28.072	-26.98 – 125.32	0.201	
Age	3.399	1.143	0.31 – 6.48	0.031	0.30
HB	-1.531	2.745	-7.02 – 3.95	0.579	
HCT	-2.426	2.599	-7.62 – 2.77	0.354	
WBCs	-9.805	10.514	-30.83 – 11.22	0.355	

D. *Quantifying Interaction effects: Findings from moderation models*

The results of the moderation regression analysis delineated in Table 4, and Figure 1. offer a nuanced understanding of the interrelations among sex, asthma severity, and ferritin levels. The model's constant is significantly different from zero, with a coefficient of 317.1352 (P < 0.0001), indicating a substantial intercept effect. The coefficient for ferritin level is -23.29 (P < 0.0001), suggesting a robust inverse association with asthma severity, where lower ferritin levels correspond to heightened asthma severity.

The sex variable itself does not present a significant effect on asthma severity (P = 0.6429), implying no direct association within the scope of this data. However, the interaction term between sex and ferritin levels is significant, with a coefficient of -12.17 (P = 0.033), highlighting a conditional effect of sex on asthma severity at specific ferritin levels. This suggested that the influence of ferritin levels on asthma severity is moderated by sex.

Table 4. Results of Moderation analysis in asthma patients and conditional effect of Sex on asthma severity at low ferritin levels

Variable	Coeff	Std. Error	P-Value	Lower limit confidence Interval (LLCI)	Upper limit confidence Interval (ULCI)
Constant	317.1352	19.14	0.0001	278.81	355.45
Ferritin	-23.29	3.99	0.0001	-31.30	-15.29
Sex	-29.00	42.21	0.6429	-153.54	95.53
Interaction	-12.17	8.40	0.0330	-37.00	- 3.650

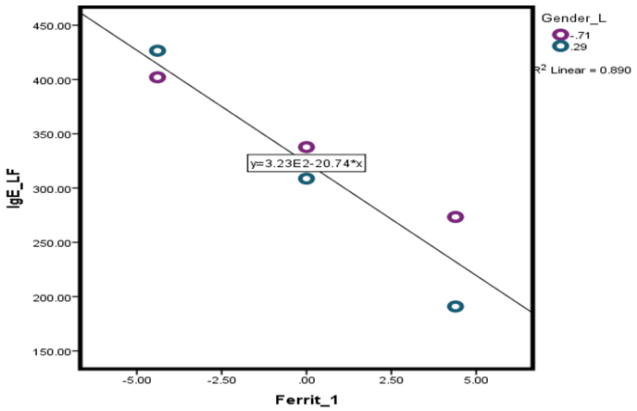

Fig. (1.): Moderating influence of Sex on the effect of low ferritin levels on asthma severity

IV. DISCUSSION

A significant public health issue is posed by the escalating incidence of anemia, asthma, and related allergic

diseases globally [19]. An association between hemoglobin (Hb) levels and an increased frequency of asthma and allergy symptoms has been documented in various studies. This study conducted in Misan, Iraq has found that a higher prevalence of anemia is exhibited in patients with allergic asthma than in healthy individuals. This observation is supported by a few epidemiological studies that have similarly reported an association between anemia and an increased incidence of asthma and allergic symptoms [20-22].

In this study, it was discovered that asthmatic patients with low ferritin levels had lower mean Hb levels (11.62 ± 3.41) and significantly higher IgE levels (327.91 ± 106.81) compared to other groups (as shown in Table 2). A surprising correlation between the incidence of anemia and IgE levels was indicated, suggesting that anemia may have a direct or indirect contribution to the risk of developing allergic asthma. The findings of this study are in agreement with those of Abdulbari et al., 2015 [23], where a significant association was concluded between low Hb levels and high levels of IgE. Additionally, a study from the US examining the association between asthma lung function in women has indicated that Hb and iron status may have a role in asthma and lung function [13].

Ferritin levels are being scrutinized as a potential risk factor for the development of asthma. In the studied group of asthmatic patients, those with low ferritin levels exhibited the lowest mean ferritin concentration (9.80 ± 2.39) among all groups, as indicated in Table 2. To assess the impact of ferritin levels on the severity of asthma, a multiple regression analysis was conducted. The results revealed that ferritin levels have a significant influence on allergic asthma, with a B-coefficient of -23.29 and a 95% confidence interval (CI) ranging from -31.30 to -15.29 (P-value = 0.0001). These findings are corroborated by several studies in the field, such as the one conducted by Rashid et al., 2019 [24] in Pakistan. This study examined the effects of anemia on the severity of asthma in females and concluded that anemia exacerbates systemic inflammatory markers, leading to increased eosinophil counts and IgE levels, which may aggravate the severity of asthma. Similarly, a study by Solomon et al., 2023 [6] investigated the prevalence of anemia and its associated factors among adult asthmatic patients in northwest Ethiopia. The study found that anemia was more common in adult asthma patients, with significant reductions in red blood cell count, hemoglobin level, and mean corpuscular hemoglobin during acute asthma exacerbations. Consequently, it is recommended that appropriate interventions be implemented to decrease the prevalence of anemia in adult asthma patients, thereby mitigating further complications and enhancing the monitoring of these patients.

The research further explored the moderating role of gender in the relationship between the independent variable (low ferritin level) and the dependent variable (IgE level). The findings indicated that there is no direct correlation between gender and the severity of asthma. Nevertheless, the interaction effect between gender and ferritin levels was significant, with a coefficient of -12.17 (P = 0.033), highlighting a conditional influence of gender on asthma severity at certain ferritin levels (as detailed in Table 4.). These results are in concordance with the findings of Schatz et al., 2003 [25], which delineated the varying relationships of gender with asthma severity; it was noted that asthma severity seems more pronounced in males aged 2 to 13 years, slightly more in females aged 14 to 22 years, and significantly more in females aged 23 to 64 years. Additionally, a study by Wang et al., 2020 [26] demonstrated that low ferritin levels are associated with heightened asthma severity, with a prevalence of 58. 7% in females, suggesting a gender-specific impact and underscoring the necessity for individualized asthma management strategies.

It is hypothesized that the underlying impact of low ferritin levels may lead to iron deficiency anemia, thereby diminishing oxygen transport to various tissues, including the lungs. This reduction in oxygen delivery could intensify asthma symptoms, particularly as the body's oxygen requirements surge during an asthma attack [27]. Additionally, iron plays a vital role in maintaining a robust immune system, influencing the proliferation and differentiation of immune cells such as T cells and macrophages, which are integral to the inflammatory response associated with asthma. Insufficient iron levels may interfere with these processes, potentially resulting in an amplified inflammatory response [12]. Moreover, research has indicated that inadequate dietary iron intake can escalate mast cell activity, culminating in airway hyper responsiveness, a characteristic feature of asthma. This implies that iron deficiency may exacerbate asthma symptoms by rendering the airways more susceptible to triggers [28].

The study acknowledges certain limitations, including the possibility that the control group could have been 2-3 times larger than the case group. The cross-sectional design of the study necessitates further longitudinal research to validate the current findings. Although patients in this study may appear to be diagnosed with asthma for the first time, it is challenging to ascertain whether they had been previously diagnosed with the condition at another healthcare facility. Lastly, due to the unavailability of comprehensive data, it was not feasible to evaluate confounding factors beyond the diseases that were excluded from this study.

V. CONCLUSION

In conclusion, this study highlights a significant association between anemia and the severity of allergic asthma, with a notable interaction between gender and ferritin levels affecting IgE levels. The findings suggest that iron deficiency, as indicated by low ferritin levels, may exacerbate asthma symptoms and inflammation, emphasizing the importance of iron management in asthma treatment strategies. Despite its limitations, the study contributes valuable insights into the complex interplay of anemia, gender, and asthma, warranting further investigation.

CONFLICT OF INTEREST

Author declares that he has no conflict of interest.

REFERENCES

[1] M. A. Bejeshk, A. Beik, A. H. Aminizadeh, F. Salimi, F. Bagheri, M. Sahebazzamani, *et al.*, "Perillyl alcohol (PA) mitigates inflammatory, oxidative, and histopathological consequences of allergic asthma in

rats," *Naunyn-Schmiedeberg's Archives of Pharmacology*, vol. 396, pp. 1235-1245, 2023.
[2] W. Burke, M. Fesinmeyer, K. Reed, L. Hampson, and C. Carlsten, "Family history as a predictor of asthma risk," *American journal of preventive medicine*, vol. 24, pp. 160-169, 2003.
[3] T. Liu, R. Valdez, P. W. Yoon, D. Crocker, R. Moonesinghe, and M. J. Khoury, "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*, vol. 11, pp. 323-328, 2009.
[4] E. R. Sutherland, "Linking obesity and asthma," *Annals of the New York Academy of Sciences*, vol. 1311, pp. 31-41, 2014.
[5] R. Polosa and N. C. Thomson, "Smoking and asthma: dangerous liaisons," *European respiratory journal*, vol. 41, pp. 716-726, 2013.
[6] Y. Solomon, N. A. Gebeyehu, G. A. Adella, G. A. Kassie, M. A. Mengstie, M. A. Seid, *et al.*, "Prevalence of anemia and its associated factors among adult asthmatic patients in Northwest Ethiopia," *BMC Pulmonary Medicine*, vol. 23, p. 222, 2023.
[7] N. Habib, M. A. Pasha, and D. D. Tang, "Current understanding of asthma pathogenesis and biomarkers," *Cells*, vol. 11, p. 2764, 2022.
[8] M. N. Garcia-Casal, S.-R. Pasricha, R. X. Martinez, L. Lopez-Perez, and J. P. Pena-Rosas, "Serum or plasma ferritin concentration as an index of iron deficiency and overload," *Cochrane Database of Systematic Reviews*, 2021.
[9] H. A. Ali, T. E. Deraz, N. I. Reyad, Y. H. Mohammed, and A. A. Husseiny, "Iron status and its relation to lung function in pediatric asthmatics: a cross-sectional study," *The Egyptian Journal of Bronchology*, vol. 16, p. 46, 2022.
[10] M. K. Ali, R. Y. Kim, A. C. Brown, J. R. Mayall, R. Karim, J. W. Pinkerton, *et al.*, "Crucial role for lung iron level and regulation in the pathogenesis and severity of asthma," *European Respiratory Journal*, vol. 55, 2020.
[11] D. Zajac, "Mineral micronutrients in asthma," *Nutrients*, vol. 13, p. 4001, 2021.
[12] F. Roth-Walter, "Iron-deficiency in atopic diseases: innate immune priming by allergens and siderophores," *Frontiers in Allergy*, vol. 3, p. 859922, 2022.
[13] E. P. Brigham, M. C. McCormack, C. M. Takemoto, and E. C. Matsui, "Iron status is associated with asthma and lung function in US women," *PloS one*, vol. 10, p. e0117545, 2015.
[14] J. Burtscher, Q. Pasha, N. Chanana, G. P. Millet, M. Burtscher, and B. Strasser, "Immune consequences of exercise in hypoxia: a narrative review," *Journal of Sport and Health Science*, vol. 13, pp. 297-310, 2024.
[15] S. Guardado, D. Ojeda-Juárez, M. Kaul, and T. M. Nordgren, "Comprehensive review of lipocalin 2-mediated effects in lung inflammation," *American Journal of Physiology-Lung Cellular and Molecular Physiology*, vol. 321, pp. L726-L733, 2021.
[16] X. Lv, M. Dong, W. Tang, J. Qin, W. Wang, M. Li, *et al.*, "Ferroptosis, novel therapeutics in asthma," *Biomedicine & Pharmacotherapy*, vol. 153, p. 113516, 2022.
[17] Z. Zeng, H. Huang, J. Zhang, Y. Liu, W. Zhong, W. Chen, *et al.*, "HDM induce airway epithelial cell ferroptosis and promote inflammation by activating ferritinophagy in asthma," *The FASEB Journal*, vol. 36, p. e22359, 2022.
[18] M. S. Allai, Z. A. Shah, K. H. Changal, M. A. Raina, and F. A. Bhat, "Association of low levels of vitamin D with chronic stable angina: A prospective case-control study," *North American journal of medical sciences*, vol. 8, p. 143, 2016.
[19] M. Masoli, D. Fabian, S. Holt, R. Beasley, and G. I. f. A. Program, "The global burden of asthma: executive summary of the GINA Dissemination Committee report," *Allergy*, vol. 59, pp. 469-478, 2004.
[20] K. Ramakrishnan and A. Borade, "Anemia as a risk factor for childhood asthma," *Lung India*, vol. 27, pp. 51-53, 2010.
[21] K. Ramakrishnan and P. Harish, "Hemoglobin level as a risk factor for lower respiratory tract infections," *The Indian Journal of Pediatrics*, vol. 73, pp. 881-883, 2006.
[22] S. Mourad, M. Rajab, A. Alameddine, M. Fares, F. Ziade, and B. Abou Merhi, "Hemoglobin level as a risk factor for lower respiratory tract infections in Lebanese children," *North American journal of medical sciences*, vol. 2, p. 461, 2010.
[23] A. Bener, M. S. Ehlayel, and Q. Hamid, "The impact of anemia and hemoglobin level as a risk factor for asthma and allergic diseases," *Indian Journal of Allergy, Asthma and Immunology*, vol. 29, pp. 72-78, 2015.
[24] H. M. Rashid, M. Khan, M. Jamal, and W. Shah, "Anemia in Asthmatic Females exaggerates the severity of inflammation in Asthma by Inducing Dyslipidemia, High levels of IgE and Absolute Eosinophil count: role of anemia on female asthmatic patient's lipidemia, IgE and eosinophil count," *Proceedings of the Pakistan Academy of Sciences: B. Life and Environmental Sciences*, vol. 56, pp. 9–14-9–14, 2019.
[25] M. Schatz and C. A. Camargo Jr, "The relationship of sex to asthma prevalence, health care utilization, and medications in a large managed care organization," *Annals of allergy, asthma & immunology*, vol. 91, pp. 553-558, 2003.
[26] E. Wang, M. E. Wechsler, T. N. Tran, L. G. Heaney, R. C. Jones, A. N. Menzies-Gow, *et al.*, "Characterization of severe asthma worldwide: data from the International Severe Asthma Registry," *Chest*, vol. 157, pp. 790-804, 2020.
[27] L. Cevhertas, I. Ogulur, D. J. Maurer, D. Burla, M. Ding, K. Jansen, *et al.*, "Advances and recent Developments in asthma in 2020," *Allergy*, vol. 75 , pp. 3124-3146, 2020.
[28] L. P. Hale, E. P. Kant, P. K. Greer, and W. M. Foster, "Iron supplementation decreases severity of allergic inflammation in murine lung," 2012.