Analytic Study of Cough and Wheezes in Children Attended to Al-Azhar Assuit University Hospital

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ABSTRACT

Background: There is a large deal of heterogeneity in the clinical appearance, duration, and course of the disease among children who wheeze and have recurrent coughs. **Objectives:** To evaluate clinically, epidemiologically and laboratory the children attended to Al-Azhar Assuit University Hospital by coughing and wheezing.

Subjects and methods: This study is a retrospective study between 1st March 2020 and the 28th February 2021 and prospective study between 1st March 2021 and 30th November 2021 and was carried out in outpatient and inpatient Pediatric Chest Unit in Al-Azhar Assuit University Hospital.

Result: Among the studied cases (Total n=324), there were 106 (32.8%) suffered from bronchial asthma, 81 (25%) suffered from pneumonia, 63 (19.4%) suffered from bronchiolitis, 27 (8.3%) suffered from COVID-19 and 47 (14.5%) suffered from other cases such as bronchitis, GERD, lung abscess and F.B. **Conclusion**: Cough in pediatric is due to multiple underlying causes, the most common are bronchial asthma, pneumonia, bronchiolitis, COVID-19, foreign body aspiration, and gastroesophageal reflux. Bronchial asthma was more prevalent among age (6-12) years but pneumonia was among age (1-6) years, bronchiolitis was among age (1-2) years and COVID-19 was among age (12-18) years. Bronchial asthma and infections as pneumonia and bronchiolitis had declined among breast feeding cases. **Keyword:** Cough, Chronic Cough, Wheezing, Children.

INTRODUCTION

Coughing is a reflex action of the lower respiratory tract in response to activation of cough receptors in the mucosa of the airways. Airway reactivity is the most typical cause of recurrent or chronic cough in children (asthma). As the pharynx, paranasal sinuses, stomach, and external auditory canal all have cough receptors, it may be necessary to look for the origin of a chronic cough somewhere outside the lungs. Inhaled dust or unpleasant gases, profuse secretions, aspirated foreign objects, cold or dry air, and an inflammatory response to infectious agents or allergic reactions are some particular lower respiratory stimuli ⁽¹⁾.

The physical examination can provide a lot of details about the origin of a persistent cough. A persistent upper respiratory condition like sinusitis is suggested by posterior pharyngeal discharge and a nocturnal cough. An enlarged chest indicates persistent airway blockage, such as in cystic fibrosis or asthma. In addition to bronchiectasis and cystic fibrosis, coarse crackles can also be a sign of an acute or subacute asthmatic exacerbation. Tracheal deviation points to pleural effusion, a mediastinal mass, or foreign body aspiration. It's crucial to provide enough time for the inspection to identify a spontaneous cough. Children who regularly cough many times per minute are more likely to develop a habit (tic) cough. Every attempt should be made to collect sputum if the cough is loose; many older kids can do so. The most frequent causes of clear mucoid sputum are allergic reactions and asthmatic bronchitis. Cloudy (purulent) sputum can indicate an asthmatic process or enhanced cellularity (eosinophilia), which is indicative of a respiratory tract infection. Sputum that is very purulent is a sign of bronchiectasis. Malodorous expectorations may

indicate anaerobic lung infection. Even when purulent, the sputum in cystic fibrosis rarely has a bad odour ⁽²⁾.

As a result of airway blockage, wheezing is the creation of a melodic continuous sound that comes from restricted airways and is audible during expiration. Due to different lung mechanics between infants and older children, wheezing is more common in the latter group. Both the size of the airway and the newborn lung's compliance have an impact on airflow obstruction. The fourth power of the tube's radius is inversely proportional to the resistance to airflow through the tube. Small-caliber peripheral airways in young infants can account for up to 50% of the overall airway resistance. The risk of wheeze increases with marginal incremental constriction, such as that brought on by viral infection-related inflammation. Infections, asthma, anomalies of the central airways, malacia of the larvnx. trachea, and/or bronchi, tracheoesophageal fistula (particularly H-type fistula), and laryngeal cleft (leading in aspiration) are some of the causes of wheezing cough ⁽³⁾. Extrinsic airway abnormalities that cause airway compression include vascular rings or slings, mediastinal lymphadenopathy brought on by infection or tumours, mediastinal masses or tumours, and esophageal foreign bodies. Intrinsic airwav abnormalities include airway hemangiomas, congenital pulmonary airway malformations (cystic adenomatoid malformations), bronchial or lung cysts, congenital ⁽⁴⁾.

Recurrent examination may be necessary to validate a history of wheezing in a kid with episodic symptoms and should be aimed towards examining air movement, ventilatory adequacy, and indications of chronic lung illness, such as fixed overinflation of the chest, and growth failure. In situations when repeated aspiration is suspected, patients should be evaluated for oropharyngeal dysphagia. It is important to look for tracheal deviation from foreign body aspiration. Wheezing caused by congestive heart failure must be ruled out. The presence of ichthyosis vulgaris, allergic rhinitis, urticaria, eczema, or allergic rhinitis all point to asthma or asthmatic bronchitis. Polyps, which can occur with allergic diseases or cystic fibrosis, should be checked for in the nose ⁽⁵⁾.

The aim of this study was to evaluate clinically, epidemiologically and laboratory the children attended to Al-Azhar Assuit University Hospital by coughing and wheezing.

PATIENT AND METHODS

Technical design:

Study design: This study is a retrospective study between 1st of March 2020 and the 28th of February 2021 and prospective study between 1st of March 2021 and 30th of November 2021.

Setting: This study was carried out in outpatient and inpatient pediatric chest unit in Al-Azhar Assuit University Hospital.

Target population: The studied data collected from retrospective cases (n=216) and prospective cases (n=108) of coughing and wheezing in outpatient and inpatient Pediatric Chest Unit in Al-Azhar Assuit University Hospital.

Inclusion criteria: Cases having cough and wheezing from 1 years' old to 18 years' old.

Exclusion criteria: Cases having cough and wheezing from below 1 month and above 18 years old. Children with a history of other diseases as heart diseases, anemia, renal, hepatic diseases and clinically significant nutritional disorder were excluded.

Methods:

1. All patients were subjected to the following:

A thorough history was taken including the following items:

- 1. Personal history (name, age, sex, address and order among siblings).
- 2. History of present illness: chest diseases, any chronic diseases
- 3. Family history: thorough history about other members specially smokers, allergy, bronchial asthma.
- 4. Perinatal history:
 - a. Prenatal history
 - b. Natal history
 - c. Postnatal history
- 5. Nutritional history
- 6. Developmental history
- 7. Past history: any chronic disease, blood transfusion or surgical Operations.

2. Full clinical examination:-

A-General examination: Built, complexion, any visible anomalies, conscious level and vital signs:

• Blood pressure, temperature, respiration rate, and heart rate.

Anthropometric measures:

• Body mass index, height, chest circumference, and head circumference.

B-Systemic examination:

Hest examination:

- Inspection: shape, symmetry, movement, respiratory distress, scar, visible pulsations, gynecomastia.
- Palpation: trachea, TVF, tenderness, transmitted sound, expansion.
- Auscultation: breath sound, bronchial, wheezes, crepitations.
- Cardiac examination: apex beat, pericardial bulge, visible pulsation apex beat, palpable thrill, heart sounds and murmurs
- Abdominal examination: abdominal enlargement, palpable organs.
- ≻Neurological examination: motor and sensory examination.
- ➤Regional examination: head and neck, upper and lower limb, back
- 3. Investigations:-
 - Chest x-ray, Chest U/S, CT chest if needed, CBC, CRP and ESR.

4. Treatment:

- Although it has been shown that cough suppressants like codeine and dextromethorphan have minimal impact, they were commonly recommended.
- Promotion of mucus expectoration by expectorants.
- Bronchodilators.
- Corticosteroids.
- Mast cells stabilizers and anti-leukotrienes if asthma and allergy were suspected.
- Antibiotics if infections were suspected.

Ethical approval:

Parents of participants, in both retrospective and prospective parts of the study, gave informed written consent, and information confidentiality was ensured. Al-Azhar Assuit, hospital manager and pediatric hospital manager of the same institution's Pediatrics and Neonatology Department, gave the authors of the study formal administrative responsibility. The research was approved by the Al-Azhar Assuit Ethics Committee of the Faculty of Medicine. During the course of this investigation, the Declaration of Helsinki for Human Beings, the international medical association's code of ethics, was observed.

Statistical analysis

The IBM SPSS (Statistical Package for the Social Sciences, 2011) software package version 20.0 (IBM Inc., Armonk, New York) was used to input data and analyse them. Number and percentage were used to describe qualitative data. The range (minimum and maximum) and mean±standard deviation (SD) were used to characterise quantitative data. P value less than 0.05 was regarded as significant.

RESULTS

This table shows that there was high statistically significant relation between the diseases and age, breast feeding, CBC abnormality, CRP abnormality and chest X-ray findings.

Parameters		Bronchial asthma	Pneumonia	Bronchiolitis	Others (bronchitis, GERD, lung abscess, F.B)	COVID-19	P value		
No.			106	81	63	47	27	.0.001*	
	%		32.8	25.0	19.4	14.5	8.3	<0.001	
A ge	1-	6 years	32	67	63	25	13		
(vears)	6-1	12 years	58	7	-	12	9	< 0.001*	
() • • • • • • •	12-	18 years	16	7	-	10	13		
Sov		Male	64	57	41	26	15	0.004	
Sex	ex Female		42	38	22	21	12	0.994	
Feeding	Brea	st feeding	41	35	28	15	9	0.027*	
history (0-2) years	Formula		65	46	35	32	18	0.037	
	Bronchial asthma		60	22	17	26	5		
Family history	Atopy (allergic rhinitis, skin and eye allergy)		20	10	10	4	8	0.658	
	Father smokers		22	15	12	9	4		
		Normal	38	28	63	22	10		
Laboratory investigations	CBC	Abnormal	(Eosinophilia) 68	(Neutrophilia) 53	-	(Leucocytosis) 25	(Lymphopenia) 17	< 0.001*	
	CDD	Normal	60	24	46	25	9	<0.001*	
	CRP	Abnormal	46	57	17	22	18	<0.001	
Chest x-rav	Pne	eumonic atches	0	34	0	0	0	0.001*	
findings	Нуре	erinflation	31	6	12	7	10	<0.001	
	Normal		28	5	23	19	5		

**Lymphopenia: lymphocytic count < 1.5x10³ cells/µl

**Eosinophilia: eosinophilic count > 500×10^3 cells/µl

**Neutrophilia: neutrophilic count > $7x10^3$ cells/µl

**Abnormal CRP: > 6 mg/l

This table shows that the most common precipitating factor of cough and wheezing were viral infections then house dust mites, father smokers, physical efforts, irritating odors, insecticides, foods, psychological factors, drugs allergy (antibiotics).

Table (2): Distribution of studied cases	s of cough and wheezing	according to precipitatin	g factors (Total n=324)
		according to proception	

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Precipitating	Studied cases (Total n=324) Yes				
factors					
	No.	%			
Viral infections	205	63.3%			
House dust mites	135	41.7%			
Father Smokers	92	28.4%			
Physical efforts	81	25%			
Irritating odors	65	20.1%			
Insecticides	58	17.9%			
Foods	50	15.4%			
Drugs allergy (antibiotics)	40	12.3%			
Psychological factors	19	5.9%			

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This table shows that cough was present in all studied cases but wheezing was present mainly in bronchial asthma and bronchiolitis cases, fever was present mainly in pneumonia and COVID-19 and dyspnea was present mainly in pneumonia and bronchiolitis cases.

Diseases	Ī	Cough	Wheezes	Fever	Dyspnea
Bronchial asthma	No.	76	91	39	62
Cases (n=106)	%	71.7%	85.8%	36.9%	58.5%
Pneumonia	No.	74	20	68	81
Cases (n=81)	%	91.4%	24.7%	84%	100%
Bronchiolitis	No.	53	58	20	48
Cases (n=63)	%	88.4%	92%	32%	76.2%
Others (bronchitis, GERD, lung abscess,	No.	33	17	30	10
F.B) Cases (n=47)	%	71%	36.2%	64.2%	21.4%
COVID-19	No.	16	0	22	5
Cases (n=27)	%	60%	-	80%	20%

Table (3): Distribution of studied cases of cough and wheezing according to symptoms (Total n=324)

This table shows that CBC, CRP, and ESR were important tools for differentiating disease from others.

D:	8	CBC	c	CRP		ESR	
Diseases		No.	%	No.	%	No.	%
Bronchial asthma	Normal	(Normal eosinophils) 38	36%	60	56.6%	79	74.6%
Cases (n=106)	Abnormal (Mean ± SD)	(Eosinophilia) 68 (1.8 ± 0.85)	64%	46	43.4%	27	25.4%
Pneumonia Batrospective	Normal	(Normal neutrophils) 28	34.5%	24	29.6%	37	45.7%
Cases (n=81)	Abnormal (Mean ± SD)	(Neutrophilia) 53 (9.2 ± 0.56)	65.5%	57	70.4%	44	54.3%
Bronchiolitis	Normal	63	100%	46	73%	63	100%
Cases (n=63)	Abnormal	0	-	17	27%	0	-
Others (bronchitis, GERD, lung abscess,	Normal	(Normal leukocytes) 22	46.8%	25	53.2%	37	78.8%
F.B) Cases (n=47)	Abnormal (Mean ± SD)	(Leukocytosis) 25 (14.5 ± 3.6)	53.2%	22	46.8%	10	21.2%
COVID-19	Normal	(Normal lymphocytes) 10	37%	9	33.3%	11	40%
Cases (n=27)	Abnormal (Mean ± SD)	(Lymphopenia) 17 (1.3 ± 0.29)	63%	18	66.7%	26	60%

Table (4).	T a h a wat a www	in mosti andi an	and an a the st	diad as as of	aarrah and		Tetel
1 able (4): 1	Laboratory	invesugation	among the su	idled cases of	cougn and	wneezing (1 otal n=524)

**Lymphopenia: lymphocytic count < $1.5x10^3$ cells/µl

**Eosinophilia: eosinophilic count > $500x10^3$ cells/µl

**Neutrophilia: neutrophilic count > 7×10^3 cells/µl

**Leukocytosis: leukocytic count > $11x10^3$ cells/µl

**Abnormal CRP: > 6 mg/l

**Abnormal ESR: > 13 mm/hr

This table shows that chest X-ray and CT chest were important for getting diagnosis of each disease but CT chest was more diagnostic.

Dadialaa		Studied Cases (Total n=324)			
Kadiolog	Ical findings	No.	%		
	Pneumonic patches	78	24%		
Chest X-Ray	Hyperinflation	153	47%		
findings	Normal	127	39%		
	COVID-19	27	8%		
CT chest findings	Abscess formation with air fluid level	6	2%		
	Longstanding F.B inhalation	16	5%		

Table (5): Distribution of studied cases of cough and wheezing according to radiological findings (Total n=324)

This table shows that pediatric COVID-19 can be handled in different categories than those defined for adults, CO-RADs 3 (Equivocal) was the most common category in pediatric COVID-19 and basal GGO was the most common site of infiltration of COVID-19 in pediatrics.

Parameter			1-6 year (n=5)	rs	6-12 (n:	6-12 years (n=9)		ears 3)
			No.	%	No.	%	No.	%
Number of j	patients (Tot	<mark>al n=27)</mark>	4	80%	5	56%	9	48%
		Right	1	20%	1	11%	4	30%
Location of o	pacities	Left	0	-	1	11%	0	-
E		Bilateral	3	60%	3	33%	5	38%
Numbers of opacities Single		Single	0	-	1	11%	4	30%
Multiple		Multiple	4	80%	4	44%	5	38%
Peripheral		1	20%	2	22%	2	15%	
Site of infiltration	on of GGO	Central	1	20%	1	11%	2	15%
		Basal	2	40%	2	22%	5	38%
Plea	ural effusion		0	-	1	11%	3	23%
	0 - Not in	terpretable	1	20%	2	22.5%	1	8%
1 - Very 1		ow (<25%)	0	-	2	22.5%	2	15%
	2 - Low	(25-50%)	1	20%	0	-	1	8%
CO-RADS	3 - Equivoo	cal (50-75%)	2	40%	3	33%	6	46%
	4 - Higl	h (>75%)	0	-	1	11%	2	15%
	5 - Ve	ry high	1	20%	1	11%	1	8%

Table (6): CT Radiological findings of children diagnosed with COVID-19 (Total n=27)

**GGO: ground-glass opacity

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Figure (1): Chest X-ray of 5 years old child showing right middle lobar pneumonia



Figure (2): CT chest of 11 years old child showing right ground glass opacities (CO-RADS 3)



Figure (3): CT chest of 6 years old patient showing left lung abscess formation

This table shows that treatment was prescribed according to underlying cause of cough and wheezing not only for symptomatic relief.

Diseases		Cough suppressants	Bronchodilators	Corticosteroids	Antibiotics	Anti- leukotrienes
Bronchial	No.	64	106	84	44	79
(n=106)	%	60.4%	100%	79.2%	41.5%	74.5%
Pneumonia	No.	68	44	59	81	-
Cases (n=81)	%	84%	54.3%	72.8%	100%	-
Bronchiolitis Cases (n=63)	No.	56	43	13	38	-
	%	88.9%	68.3%	20.6%	60.3%	-
Others (bronchitis,	No.	43	17	12	37	-
GERD, lung abscess, F.B) Cases (n=47)	%	91.5%	36.2%	25.5%	78.7%	-
COVID-19	No.	27	11	27	27	-
Cases (n=27)	%	100%	40.7%	100%	100%	-

 Table (7): Type of treatment among the studied cases of cough and wheezing (Total n=324)

DISCUSSION

In the present study we found that the mean age of studied cases was 7 years (± 4.98 SD) with range (1-18) years, the age from (1-6) years was 205 (63.3%), the age from (6-12) years was 73 (22.5%), the age from (12-18) years was 46 (14.2%). Among the studied cases there were 154 (47.5%) females and 170 (52.5%) males. The results of another study indicated that, with a mean age of 14.1 \pm 0.7 years and a range of 13 to 17 years, 46% of cases were male and 54% were female ⁽⁶⁾.

In the present study we found that bronchial asthma had more prevalence among (6-12) years which were 58 cases, among (1-6) years were 32 cases and among (12-18) years were 16 cases. Also, bronchial asthma had more prevalence among males which were (64) cases than females which were (42) cases and among these bronchial asthma cases there were 60 (57%) who had family history of bronchial asthma, 20 (19%) had family history of atopy (allergic rhinitis, skin and eye allergy) and 22 (21%) had father smokers. In another study, it was shown that among asthmatic students, a family history of asthma was substantially related with asthma (p 0.0001) (5). Moreover, our findings concur with those of earlier research by Zedan et al. (7) and FuatKalyoncu et al. (8). As asthma is a condition impacted by both hereditary and environmental factors, this can be explained.

According to another study, guys had more severe and frequent asthma than girls did ⁽⁹⁾. Whereas **Landau** *et al.* ⁽¹⁰⁾ discovered that beyond the age of 6 years, gender differences in asthma prevalence were less noticeable. Moreover, **Hsu** *et al.* ⁽¹¹⁾ discovered that 30% of their patients' symptoms began before the age of 14. In another research, 209 youngsters, including 106 (8.6%) boys and 103 (6.9%) girls, were diagnosed with asthma. They were 7.4 \pm 2.1 years old on average. Passive smoking, unsuitable housing, and a positive family history were all mentioned by 67.6%, 47.8%, and 81.3% of patients, respectively ⁽⁷⁾.

In the present study we found that among the studied bronchial asthma cases, there were 41 cases had breast feeding but 65 cases had artificial formula so bronchial asthma was declined among breast feeding cases. According to another study, subjects with asthma were more likely to be male, have a history of asthma in their parents, and have been breastfed. There was still a very low incidence of asthma among artificial milk feeders. Also, they discovered a substantial correlation between the occurrence of asthma and the impact of nursing ⁽¹²⁾. There have been mixed results regarding breastfeeding's impact on asthma. Breastfeeding was shown to have a protective impact against asthma in various research, according to two prior studies'

findings ^(13,14), whereas other studies failed to establish any associations like ⁽¹⁵⁻¹⁷⁾.

In the present study we found that among the studied cases there were 130 (40%) who had family history of bronchial asthma, 52 (16%) had family history of atopy (allergic rhinitis, skin and eye allergy) and 62 (19%) had father smokers. According to the results of another research, 6.2% of the pupils were asthmatic. Age, gender, or place of residence were not substantially linked with asthma (rural or urban). Asthma was substantially linked (p 0.0001) with the occurrence of one or more allergic illnesses (skin, nasal, ocular, and other allergies to food or beverages) ⁽⁶⁾. Another research conducted in Egypt discovered that atopic dermatitis, allergic rhinitis, or food allergies were present in 53.3% of the asthmatic children who were examined ⁽¹⁸⁾. According to a different study, cigarette smoke is the main indoor irritant and a significant trigger of asthma symptoms in both children and adults (19)

The present study showed that among the studied COVID-19 cases there were 27 (100%) treated with cough suppressants, 11 (40%)with bronchodilators, 27 (100%) with corticosteroids, 27 (100%) with antibiotics, among the studied bronchial asthma cases there were 64 (60.4%) treated with cough suppressants, 106 (100%) with bronchodilators, 84 (79.3%) with corticosteroids, 44 (41.6%) with antibiotics, 79 (74.6%) treated with anti-leukotrienes, among the studied bronchiolitis cases there were 56 (89%) treated with cough suppressants, 43 (68.3%) with bronchodilators, 13 (20.7%) with corticosteroids, 38 (60.4%) with antibiotics, among the studied pneumonia cases there were 68 (84%) treated with cough suppressants, 44 (54.4%) with bronchodilators, 59 (73%) with corticosteroids. 81 (100%) with antibiotics and among the studied others cases there were 43(92%)treated with cough suppressants, 17 (36%) with bronchodilators, 12 (25.6%) with corticosteroids, 37 (78.8%) with antibiotics.

Nine patients were not on any medication at the time of recording, according to another research. Beta2sympatiomimetica, inhaled glucocorticoids, or antibiotics had all been administered to the other subjects (20). Just nine out of 36 patients in another research were not treated, as was demonstrated. The other patients were given various medications, including 2 antibiotics, 21 salbutamol, 21 ipratropium bromide, 15 intravenous prednisolone, 3 secretagogue, 1 antitussive, 16 NaCl 0.9%, and 11 more oxygen⁽²¹⁾. The NA+ group in the other trial utilised noticeably (P 0.01) more maintenance medicine than the NA- group, including inhaled corticosteroids, cromolyn sodium, and ketotifen ⁽²²⁾. According to another research, inhaled corticosteroids (ICSs) are the first-line treatment for most patients with mild to moderate asthma, and low- to medium-doses of ICSs by themselves are sufficient to manage their symptoms (23). For patients who are not effectively managed on low-medium dosage ICSs, LABAs serve as an additional treatment ⁽²⁴⁾. The barriers to LABAs' usage on a larger scale in our society include their cost and worries about adverse effects.

CONCLUSION

Cough in pediatrics is a common presenting complaint and is due to multiple underlying causes, the most common are bronchial asthma, pneumonia, bronchiolitis, COVID-19, foreign body aspiration, and gastroesophageal reflux. Bronchial asthma was more prevalent among age (6-12) years but pneumonia was among age (1-6) years, bronchiolitis was among age (1-2) years and COVID-19 was among age (12-18) years. Bronchial asthma and infections as pneumonia and bronchiolitis had declined among breast feeding cases. For making a diagnosis, a thorough history-taking and physical examination are frequently advised, however a CT chest scan is more diagnostic. The COVID-19 findings for children can be addressed in categories that are distinct from those for adults. The CT chest abnormalities can increase pediatric COVID-19 awareness in symptomatic instances up until the realtime PCR results are available. The underlying ailment is treated, and there is little support for just providing drugs to treat symptoms.

RECOMMENDATIONS

- 1. Attempts should be taken to keep children with persistent coughs away from triggers such cigarette smoke, viral illnesses, and household dust.
- 2. Encouragement of mothers for breast feeding as it gives protection against respiratory tract infections and asthma incidence declines
- 3. If there are symptoms of the lower respiratory tract, a chest radiograph should be taken into consideration.
- 4. CT chest should be done for COVID-19 cases to categorize cases then treatment, precautions and warnings started according to each category.
- 5. Bronchitis, pneumonia, bronchiolitis, asthma, and other common specific causes of acute cough should be treated according to evidencebased guidelines.

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