

Original Research Article

A case series of cyclic vomiting syndrome in children at pediatric gastroenterology clinic in Benghazi medical

ABSTRACT

Background: Cyclic vomiting syndrome (CVS) is a functional disorder characterized by repeated episodes of sudden onset of intense vomiting that is followed by symptom-free periods. The diagnosis is based on the fulfillment of Rome IV criteria. The Cyclic vomiting syndrome shares similar features to migraine headaches. It is under-recognized and often misdiagnosed with significant delays in therapy.

Aims: To evaluate the clinical characteristic of pediatric patients diagnosed with cyclic vomiting syndrome in our institution and their response to treatment.

Patients and Methods: A prospective case series of 13 pediatric patients with cyclic vomiting syndrome seen between period of November 2018 to November 2020 at pediatric gastroenterology outpatient's clinic in Benghazi medical center. All relevant data including; age and sex, age of presentation, duration of symptoms, age at diagnosis, presence of aura or prodromal symptoms, patient or family history of headache, treatment and their response to treatment were collected.

Results: The mean age for diagnosis was 112.2 ± 37.7 months. 46.2% of patients had recognizable prodromal symptoms. Patients with CVS had intense nausea and persistent vomiting that requiring hospitalization. In 44.4% of patients had stopped the episodes as a response to propranolol.

Conclusion: Cyclic Vomiting Syndrome (CVS) is a functional, an under-recognized, and misdiagnosed episodic. The illness is characterized by stereotypical pattern of vomiting leading to frequent hospitalizations.

Keywords: Cyclic vomiting syndrome, Rome IV criteria, stereotypic vomiting, children.

1. INTRODUCTION

Cyclic vomiting syndrome (CVS) is an under-recognized and frequently misdiagnosed episodic illness. It is a chronic functional illness that can occur in both children and adults. It is characterized by sudden episodes of intense nausea and vomiting which last for hours to days, alternate with symptom-free periods which last for weeks to months [1,2]. The symptoms of this illness can lead to repeated emergency visits, frequent hospitalizations, school absenteeism, and decreased quality of life. It is often misdiagnosed due to a lack of diagnostic tests and the unappreciated pattern of recurrence. The incidence of CVS is unknown to adult patients but is cited as 3%–14% [1] and affects between 0.04% – 2% of

pediatric patient populations [3, 4]. The recent population-based study reported a prevalence of up to 6.1% in children under 2 years old [5]. There is a slight predominance of girls over boys (86 VS 57%) [6] with a mean age of onset of 5 years[7] and the mean age at diagnosis is 8.2 to 9.5 years[8].

The etiology and pathogenesis of CVS are poorly understood, but it shares similar features with migraine headaches, it may be considered as a migraine variant. The International Classification of Headache Disorder (ICHD III beta) [9] considers CVS as a pediatric migraine variant. The Rome IV Criteria included CVS among the functional gastrointestinal illnesses [10-12]. Other several theories are under investigation, including autonomic [13] and hypothalamic-pituitary-adrenal axis hyper-reactivity[14], and mitochondrial dysfunction[15-17].

CVS is characterized by recurrent, stereotypic episodes of intense nausea and vomiting for a period ranging from hours to days, that are separated by symptom-free intervals which last weeks to months [18]. 'Stereotypic' episode means that each episode is similar within individuals as to the time of onset, intensity, duration, frequency, and associated symptoms and signs. CVS typically has four phases: prodromal phase (pre-emetic), emetic phase, recovery phase, and asymptomatic or inter-episodic phase. Several patients have an aura in the prodromal phase lasting for several minutes and sometimes last up to hours, frequently consisting of abdominal pain, lethargy, sweating, or salivation. The emetic phase usually consists of intense nausea associated with frequent vomiting that tends to start in the early morning [19,20]. In the recovery phase, vomiting stops and appetite improves, and activity recovers then patients return to baseline health between episodes.

A number of CVS patients can identify the triggering conditions that can trigger the onset of the cycle of vomiting episodes. Triggers include negative and positive psychological stress or physical stress (infections, lack of sleep) the onset of menses which is also known as (catamenial CVS), and some food items (e.g. chocolate, cheese, monosodium glutamate) [19,21-23]

The diagnosis of CVS should be made after excluding other causes of vomiting and the typical clinical presentation as described by the Rome IV criteria. Rome IV criteria define CVS as stereotypic episodes of vomiting with the following characteristics: 1) presence of at least two acute episodes of vomiting in the preceding six months, 2) each episode of vomiting persisting for less than one week, 3) at least one week of an interval between episodes of vomiting, and 4) an absence of vomiting between episodes [24,25].

There is no curative treatment for CVS. Treatment goals are to reduce the severity and frequency of episodes and to improve the quality of life. Treatment includes identification and avoids triggers. During acute episodes, supportive therapy including IV rehydration and high-dose ondansetron is also recommended with psychological support to the patient and family. [24,25]

The NASPGHAN consensus statement recommendations of prophylactic therapy include the use of cyproheptadine (a first-generation antihistamine) or amitriptyline a tricyclic antidepressant as the first line. Propranolol (a beta-blocker) is used as the second line of prophylactic treatment. In patients with infrequent attacks, triptans should be considered as an abortive agent for those more than 12 years. [26, 27]

Many studies have suggested that anxiety and stress play a significant role in the onset and perpetuation of symptoms of CVS [27-29]. Our own clinical experience would suggest that the provision of a diagnosis and information about the CVS greatly alleviate the burden of

illness for these children and their families. Furthermore, studies regarding cyclic vomiting syndrome in children are rare in Libya. The aim of this study is to describe the clinical characteristic of pediatric patients diagnosed with cyclic vomiting syndrome in Benghazi medical center and their response to treatment.

2. METHODOLOGY

A prospective study was conducted at the pediatric gastroenterology outpatient clinic in Benghazi Medical Center. In this study, we reviewed all patients' medical records who were diagnosed with CVS based on Rome IV criteria. During the period of November 2018 to November 2020, we found thirteen pediatric patients fulfilling who meet the Rome IV criteria.

2.1 Consent

We contacted the head pediatric gastroenterology outpatient clinic department at Benghazi medical center to explain the goal of this study, and we gained permission to review the patients' medical records. Next, we contacted the parents whose children meet our criteria to explain the goal of this study. Then a consent form was signed by the parents allowing the use of their children's data in the study and agree to the publication of this manuscript.

2.2 Data Collection

Data was collected via the form created by the researcher based on previous studies [27-29]. Thirteen of the patient medical records were reviewed and recorded data on the form. The form contained demographic data such as age and gender. In addition; clinical data such as laboratory tests were collected.) All relevant data including age and sex, age of presentation, duration of symptoms, age at diagnosis, presence of aura or prodromal symptoms, patient or family history of headache, treatment, and their response to treatment were collected.

2.3 Data Analysis

It was executed using the Statistics Package Social Science (SPSS) program version 20. Continuous variables were presented as means, median, standard deviation, and range. Categorical variables were reported with the use of proportions and percentages. Also, column charts and pie charts were used to describe and compare variables.

3. RESULTS

A total of 13 patients were diagnosed with CVS during the study period. Two third of them were male (61.2%). Almost all of the patients were older than 5 years in age. The mean age at onset of symptoms was 86.6 ± 38.9 months, whereas the mean age for diagnosis was 112.2 ± 37.7 months; as shown in Table 1. About 46% of patient reported to have recognizable prodromal symptoms; as shown in Table 2.

Table 1. Characteristics of patients

Variable	No.	%
Gender		
Male	8	61.5%
Female	5	38.5%
Family History Migraine		
Yes	8	61.5%
No	5	38.5%
Age in months		
Mean $\pm$ SD	118 $\pm$ 34.1	
Median	120	
Minimum–maximum	66-163	
Age at onset of symptoms (months)		
Mean $\pm$ SD	86.6 $\pm$ 38.9	
Median	81	
Minimum–maximum	36-144	
Age at diagnosis (months)		
Mean $\pm$ SD	112.2 $\pm$ 37.7	
Median	120	
Minimum–maximum	63-163	
Number of previous admissions		
Mean $\pm$ SD	8.5 $\pm$ 12.3	
Median	3	
Minimum–maximum	0-40	

Positive family history of migraine in 8 patients (61.5%) and negative in 5 patients (38.5%). As Shown in Table 1 and Figure 1.

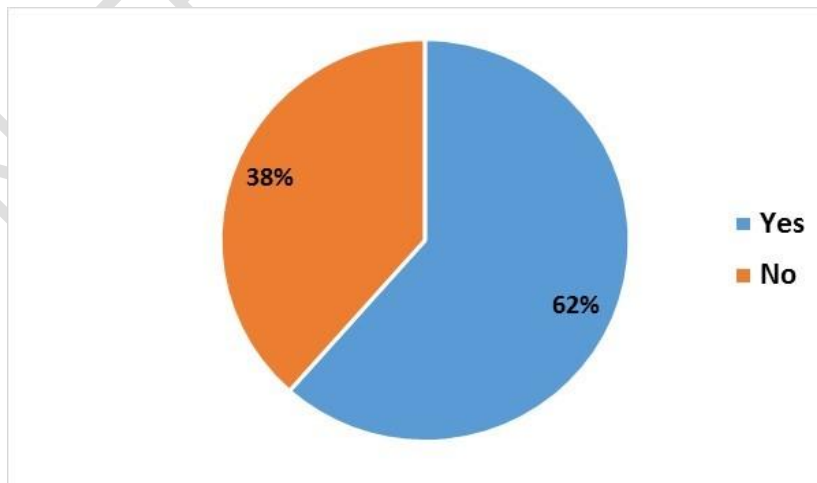


Fig. 1. Family History Migraine

The episodes of CVS were stereotypic among all patients with vomiting episodes for each patient last the same duration every time and each episode recurred at same interval each time in the same patient. Among our patients, interval between episodes of cyclic vomiting was 8.3 ± 5.7 months. The mean duration of each episode was 4.7 ± 1.3 days (Table 2).

Four patients (30.7%) had infrequent episodes of CVS and they received supportive management only and they didn't receive any prophylactic treatment. Nine patients (69.2%) had too frequent CVS episodes, a prophylactic treatment with propranolol have been started for them. Only one patient (11.1%) didn't respond the prophylactic treatment with propranolol and shifted to topiramate, 4 patients (44.4%) the episodes stopped and 4 patients (44.4%) the frequency of the cycles reduced. As shown in Table 2 and Figure 2.

Table 2. Clinic data of patients

Variable	No.	%
Prodrome symptoms		
Yes	6	46.2%
No	7	53.8%
Symptoms during prodrome		
Salivation	1	7.7%
Abdominal pain	7	53.8%
Abdominal pain and headache	5	38.5%
Prophylactic		
No treatment	4	30.7%
Propranolol	9	69.2%
Response to treatment for 9 patients		
Cycles stopped	4	44.4%
Cycles frequency decreased	4	44.4%
Not respond to propranolol (other treatment)	1	11.2%
delay DX (months)		
Mean $\pm$ SD	25.6 $\pm$ 17.7	
Median	24	
Minimum–maximum	2-48	
Duration of episode (days)		
Mean $\pm$ SD	4.7 $\pm$ 1.3	
Median	5	
Minimum–maximum	3-7	
Inter-episode interval (months)		
Mean $\pm$ SD	8.3 $\pm$ 5.7	
Median	8	
Minimum–maximum	2-24	

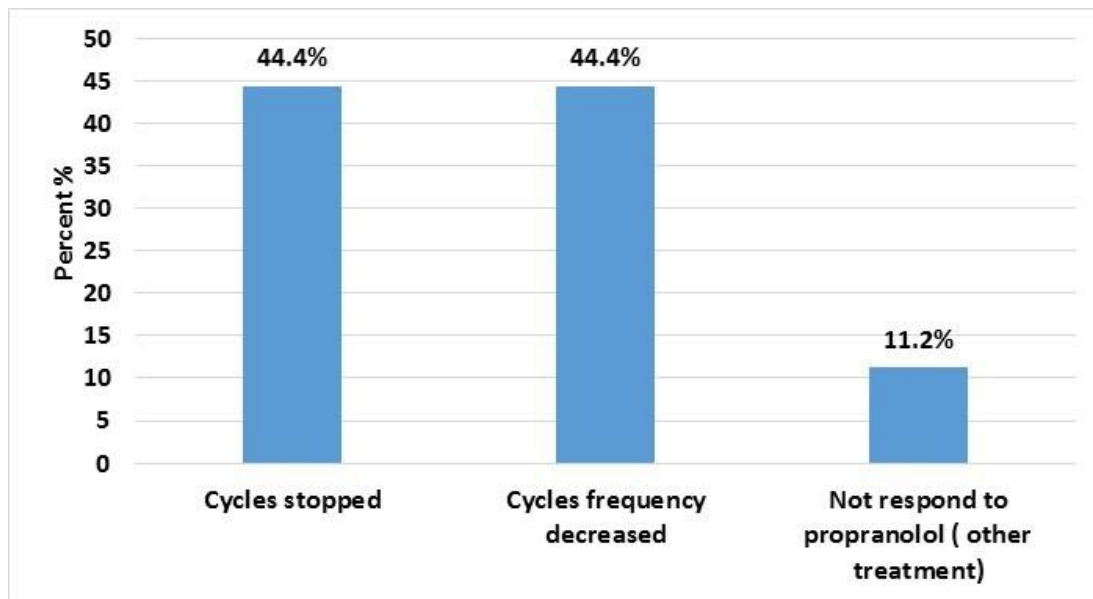


Fig. 2. Response to propranolol treatment

4. DISCUSSION

A total of 13 patients were diagnosed with CVS during the study period. Two third of them were male (61.2%) which is opposite to other studies that showed female were more affected than male [27,28,29]; the discrepancy between our study result and result's in literature may be due to the small sample size in our study. Almost all of the patients in our study were older than 5 years in age which is consistent with other studies in different population [28,29,30].

The mean age at onset of symptoms was 86.6 ± 38.9 months (7.2 ± 3.2 years) which was similar to that reported by Khalil and Liao et al. [27, 29], whereas the mean age for diagnosis was 112.2 ± 37.7 months (9.3 ± 3.1 years). The mean interval from onset of symptoms to the accurate diagnosis was 25.6 ± 17.7 months (2.1 ± 1.4 years), which was comparable with that reported by Liao et al. [29]

46.2% of patient reported to have recognizable prodromal symptoms which was more than that reported in patients of other studies (25–38%), [31, 28] and less than reported by Khalil (two third of patients). [27]

Prodromal symptoms that reported were abdominal pain in 7 patients (53.8%), headache with abdominal pain reported by 5 patients (38.5%) and excessive salivation reported by one patient (7.7%).

Positive family history of migraine in 8 patients (61.5%) which seemed higher than that reported by Ertekin et al. and Ziqing et al. (29.2% and 11.9%) [28, 30]; the discrepancy between our study result and result's in literature may be due to the small sample size in our study.

The episodes of CVS were stereotypic among all patients with vomiting episodes for each patient last the same duration every time and each episode recurred at same interval each time in the same patient. Among our patients, interval between episodes of cyclic vomiting was 8.3 ± 5.7 months. The duration of attack ranged from 3 to 7 days (median: 5 days) which was similar to that reported by Ertekin et al. [28]

Patients with CVS had intense nausea and persistent vomiting that requiring hospitalization, among our patient mean of admission to the hospital was 8.5 ± 12.3 times. 4 patients (30.7%) had infrequent episodes of CVS and they received supportive management only and they didn't receive any prophylactic treatment. Nine patients (69.2%) had too frequent CVS episodes, a prophylactic treatment with propranolol have been started for them. Only one patient (11.1%) didn't respond the prophylactic treatment with propranolol and shifted to topiramate, 4 patients (44.4%) the episodes stopped and 4 patients (44.4%) the frequency of the cycles reduced. Khalil AF reported that the response rate to propranolol was 90.1% and similarly Haghighat et al in a large series reported that the response rate to propranolol was 92% without significant adverse effects [27, 31,32].

Limitations: This study had some limitations, firstly the smaller number of patients who diagnose with CVS based on Rome IV criteria. And information on the outcome of CVS in children is limited. Also, The limited research about cyclic vomiting syndrome in children in Libya.

5. CONCLUSION

Cyclic Vomiting Syndrome (CVS) is a functional, an under-recognized and misdiagnosed episodic illness characterized by stereotypical pattern of vomiting leading to frequent hospitalizations, multiple comorbidities, and poor quality of life. The treatment of CVS remains challenging. Pediatricians should be aware to this under-recognized illness and consider it in the differential diagnosis of recurrent episodic vomiting in children.

CONSENT

All respondents' parents who agreed to participate in the study were required to initialize the informed consent form.

ETHICAL APPROVAL

The principle of Medical Research Ethics guidelines from the Faculty of Medicine, University of Benghazi, were observed during this study.

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