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Portal hypertension among Egyptian children and adolescents (single center study).

Reham I Abdelmageed[1], Lerine B El Shazli[1], Mayada A Fathy[2], Asmaa W Abdelaziz[1*]

[1]Department of Pediatrics, Ain Shams University, Cairo, Egypt

[2]General Practitioner, Ministry of Health, Cairo, Egypt

Abstract

Portal hypertension is a clinical syndrome in which the portal venous pressure gradient between the portal vein and inferior vena cava exceeding 5 mmHg. Clinically significant portal hypertension is diagnosed when clinical manifestations of the disease appear or the portal pressure gradient exceeding 10 mmHg. For better management, it is important to determine the underlying cause. This study aimed to evaluate the aetiology, presentation and quality of life in pediatric portal hypertension patients.

This cross-sectional study was done on ninety-one consecutive cases of portal hypertension enrolled from 2016 to 2019. Demographic data, etiology, clinical presentation, endoscopic interventions, and quality of life were all assessed. The mean age of participants was 5.55 ± 4.30 years with a male to female ratio of 1.5:1. Out of 91 children, 56.1% developed portal hypertension due to extrahepatic causes and 42.9% due to hepatic causes. In extrahepatic causes portal vein obstruction was the most common aetiology representing 39.6% Splenomegaly was the commonest presentation of PHT and esophageal varices were the commonest complication. QoL scores, total and individual domains, were lower in all our PHT children.

Conclusion: Extra hepatic portal vein obstruction was the most common etiology of portal hypertension in studied cases. Poor QOL was reported in all patients irrespective of the etiology of portal hypertension.

Keywords: Portal hypertension, Egyptian children and adolescents, Extrahepatic disease, Quality of life.

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Introduction

Portal Hypertension (PHT) is a clinical syndrome in which the portal venous pressure gradient between the Portal Vein (PV) and inferior vena cava exceeding 5 mmHg [1]. Portal hypertension is considered one of the major problems which count morbidity and mortality in children with liver disease. Portal hypertension results in the formation of portal-systemic collaterals that shunt a portion of the blood flow of the portal to the systemic circulation [2].

By passing the liver; it can arise from disorders with blood flow at any level within the portal system [3]. Usually, portal hypertension is associated with an increased cardiac index, hyperkinetic syndrome, characterized by hypervolemia, hypotension, and reduced systemic vascular resistance. Moreover, several studies have reported the pattern of portal hypertension to be different in children and adults; in adults its pattern is mostly intrahepatic, whereas the pattern is extra-hepatic in children [4].

Causes of portal hypertension can be classified according to their anatomical location: prehepatic (involving the splenic–portal–mesenteric venous axis), intrahepatic, and post-hepatic [5]. In clinical practice, a bleeding episode from esophageal varices is a major clinical event that is associated with significant adverse sequelae [6]. The major complications of portal hypertension are variceal hemorrhage, ascites, hypersplenism, hepatopulmonary syndrome, porto-pulmonary hypertension, hepatorenal syndrome, and hepatic encephalopathy which can affect the quality of life of the children. This work aimed to explore the etiology, presentation, complications, and management of pediatric patients with portal hypertension.

Methods

This cross-sectional study included 91 patients diagnosed with portal hypertension based on combined clinical and radiological evidence from 2016 to 2019. Children with a history of significant developmental delay, psychological issues, or taking other medications confounding responses to assessments were excluded from the study. Written informed consents were obtained from participating children and or their parents; also ethical approval was obtained from the research ethics committee at the faculty of medicine, Ain Shams university hospital (FWA000017585).

All patients were subjected to: Full history taking including demographic data, history stressing on admission in Neonatology Unit (NICU), duration of NICU stays, exchange transfusion, umbilical catheterization, and previous blood transfusion). Family history also was evaluated including a history of liver disease, sibling death from the same disease, and consanguinity. Clinical evaluation: including etiology of

portal hypertension, symptoms, and signs of portal hypertension like hematemesis, abdominal distension, jaundice, symptoms of hepatic encephalopathy, and chronic liver disease. Laboratory investigations: were done to confirm and evaluate the etiology and complications of portal hypertension. Patients were subjected to routine laboratory investigations including complete blood count. Liver enzyme: Alanine Transaminase (ALT), Aspartate Aminotransferase (AST), albumin, bilirubin, Prothrombin Time (PT), and International Normalized Ratio (INR).

Upper GIT endoscopy was performed to detect and grade the presence of esophageal varices and Portal Hypertensive Gastropathy (PHG), varices were graded according to japanese research for portal hypertension classification system as follows: grade Gr-I: Small esophageal varices which flatten with insufflation or minimally protrude into the esophageal lumen, Gr-II: Moderated sized varices with minimal obscuring of the gastroesophageal junction, Gr-III: Large varices showing luminal prolapse substantially obscuring the gastroesophageal junction ,and Gr-IV: Very large esophageal varices that completely obscuring the gastroesophageal junction and do not flatten on insufflation [3].

Quality of life was evaluated after obtaining informed consent using PedsQL™-4.0 generic core scale, Arabic version: questionnaire (face to face interview with parents and patients using structured questionnaire and the information collected include the effect of the disease (PHT) on physical, social, psychological, and school performance of patients). It consists of four scales divided into 23 items assessing the level of psychosocial and physical functioning of children. There are 8 items of physical functioning.

Three subscales are categorized into psychosocial functioning: social, emotional, and school functioning, each consisting of 5 items. The instructions ask for the degree of a problem during the previous month for each item. The Likert response scale of five points is used (0: Never a problem, 4: Almost always a problem). Items are reversed and translated to a scale of 0-100 linearly, with higher scores indicating better HRQOL. Scale scores are computed as the sum of items divided by the number of items answered (accounting for missing data) [7]. Linguistic validation and psychometric properties are well documented [8].

Statistical Analysis

Using IBM SPSS software package version 25, the data was fed to the computer and analyzed. Numbers and percentages were used to define qualitative results. Parametric numerical data were given as mean ± Standard Deviation (SD), while frequency, and percentage (%) for non-numerical data. The tests used were a Chi-square test for categorical variables to be compared between different groups. Fisher's Exact: Correction for chi-square when more than 20% of the cells are predicted to count less than 5. F-test (ANOVA): For normally quantitative variables, to compare between more than two groups. $P<0.05$ is considered statistically significant.

Results

Patients' characteristics

Table 1 showed some of the patients' characteristics. In the present study, 91 patients were diagnosed with portal hypertension. Their mean age was 5.55 ± 4.30 years. More than 70% of patients were males, and from a rural area, it was found that 44 (48.4%) patients out of 91 were admitted to NICU (72% of them were diagnosed with PV obstruction versus 11.4% were diagnosed as CHF), five patients 5.5% had a history of exchange transfusion, and nine 9.9% had a history of umbilical catheterization.

As for the family history of the studied patients, thirty-three patients had positive consanguinity, eight patients (5 were diagnosed with CHF, 3 were cryptogenic cirrhosis) had a positive family history of liver diseases, only two CHF patients had a positive family history of sibling death of the same disease. In this study, PV obstruction was the most common cause of PHT 39.6%. Other causes of PHT were CHF 23.1%, budd chiari syndrome 16.5%, liver cirrhosis 13.2%, biliary atresia 3.3%, autoimmune hepatitis 3.3%. Patients with PV obstruction presented at earlier age (4.01 ± 3.46) year, followed by cases with CHF (5.86 ± 3.71) years. Cases with Budd Chiari and cryptogenic cirrhosis presented at an older age (12.86 ± 4.95 and 9.22 ± 5.40) respectively ($p<0.001$).

Patients characteristics	No.	%
Sex		
Male	67	73.6
Female	24	26.4
Age		
Min– Max	5 months –16 years	
Mean ± SD	5.55 years ± 4.30	
Residence		
Rural	65	71.4

Urban	26	28.6
NICU admission	44	48.4
Duration of NICU admission (days)		
Min– Max	5.0–30.0	
Mean ± SD	13.69 ± 6.66	
Exchange transfusion	5	5.5
Umbilical catheterization	9	9.9
Etiology		
PVT	36	39.60%
CHF	21	23.10%
Budd chiari syndrome	15	16.50%
Cirrhosis	12	13.20%
Extrahepatic biliary atresia	3	3.30%
Autoimmune hepatitis with secondary hepatic fibrosis	3	3.30%
Endoscopic findings		
No varices	3	3.5%
Varices	73	85.9%
Grade I–Grade II	33	38.8%
Grade III	39	45.9%
Portal hypertensive gastropathy	9	10.6%
Pharmacological treatment	89	97.8%
Endoscopic therapeutic modalities		
Band ligation	44	48.4%
Sclerotherapy+band ligation	14	15.4%
Others		
Balloon tamponade	3	3.3%
Splenectomy	3	3.3%

Table 1. Patients characteristics.

Eighty-five patients underwent endoscopy, more than 85% of them had varices distributed as 38.8% showed grade I-II while 45.9% showed grade III varices, and 10.6% of cases had portal hypertensive gastropathy.

As for therapeutic endoscopic modalities, 58 patients underwent therapeutic endoscopic procedures in the form of band ligation in 44 cases and combined sclerotherapy and band ligation in 14 cases.

B blockers were prescribed in 89 patients to decrease splanchnic blood flow.

Clinical profile

As regard initial clinical presentation, most PV obstruction patients were presented by hemostasis and melena, while abdominal distension was commonly presented in cirrhosis, CHF and, budd chiari patients.

As regards the clinical signs of PHT, splenomegaly was reported in all cases of different etiology.

Varices were the major complication of PHT which occurred in 90.1% of cases, followed by pancytopenia with splenomegaly in 60.4%, ascites in 26.4%, and liver failure in 2.2% (Table 2).

Clinical presentation	PV obstruction (n=36)		Cirrhosis (n=12)		Budd chiari (n=15)		CHF (n=21)		X^2	FEp
	No.	%	No.	%	No.	%	No.	%		
Abdominal distention	30	83.30%	11	91.70%	11	73.30%	19	90.50%	2.517	0.472
Ascites	27	75.00%	12	100.00%	5	33.30%	11	52.40%	5.03	0.111
Hematemsis and melena	35	97.20%	11	91.70%	6	40.00%	8	38.10%	23.687	0
Hepatomegaly	13	36.10%	12	100.00%	5	33.30%	19	90.50%	3.553	0.201
Jaundice	2	5.60%	4	33.30%	6	40.00%	8	38.10%	22.891	0
Pancytopenia with splenomegaly	9	25.00%	7	33.30%	6	40.00%	2	16.70%	6.718	0.081
Splenomegaly	36	100.00%	12	100.00%	15	100.00%	21	100.00%	----	-----
Varices	35	97.20%	20	95.20%	14	93.30%	11	91.70%	0.83	0.842

Table 2. Clinical presentation and complications in different etiological of PHT patients: X2: Chi square test; FE: Fisher's Exact test.

Laboratory profile

Among the studied cases, 91.2% suffered from anemia and 73.6% suffered from thrombocytopenia, their hemoglobin ranged from 6-12.6 g/dl, and their platelets number ranged from 54-375 (× 103 cells/µl). It was found that the level of AST was increased in cirrhotic patients in 100% of cases versus 19.4% of PV obstruction cases and 33.3% of CHF cases and 33.3% of BCS, which was statistically significant while, there was preservation of other liver functions in the majority of cases of PV obstruction (Table 3).

Liver functions	CHF (n=21)		PV obstruction (n=36)	Budd chiari (n=15)		Cirrhosis (n=12)	X^2	P		
	No.	%	No.	%	No.	%			No.	%
AST (u/l)										
Normal	14	66.70%	29	80.60%	10	66.70%	0	0	23.129	0
Increased	7	33.30%	7	19.40%	5	33.30%	12	100.00%		
ALT (u/l)										
Normal	17	81.00%	30	83.30%	8	53.30%	0	0	18.893	0
Increased	4	19.00%	6	16.70%	7	46.70%	12	100.00%		
PT (sec.)										
Normal	15	71.40%	36	100%	14	93.30%	8	66.70%	14.707	0.002
Prolonged	6	28.60%	0	0%	1	6.70%	4	33.30%		
T. Bilirubin (mg/dl)										
Normal	16	76.20%	33	91.70%	3	20%	3	25.00%	22.885	0
Increased	5	23.80%	3	8.30%	12	80%	9	75.00%		
Albumin (g/dl)										
Normal	13	61.90%	33	91.60%	8	53.30%	3	25.00%	10.015	0.018
Decreased	8	38.10%	3	8.40%	7	46.70%	9	75.00%		

Table 3. Liver functions in different etiologies of PHT. X2, p: X2 and p values for Chi square test for comparing between the two groups. *: Statistically significant at $p \leq 0.05$; AST (u/l): Normal (18-63); ALT (u/l): Normal (20-60); PT (sec.): Normal (11-14); Alb (g/dl): 3.1-4.8; Bil (mg/dl): Normal (0.2-1.3).

Regarding quality-of-life score

It was noted that there was a lowering in all health domains (Table 4). Moreover, QOL scores total and in individual domains, were significantly lower in children with hypersplenism in comparison to children without hypersplenism (Table 5).

		Range	Mean ± SD
Physical	PVT	50–75	61.97 ± 7.31
	CHF	50–80	64.57 ± 9.55
	Budd chiari	50–80	64.27 ± 8.13
	Cryptogenic cirrhosis	75–80	77.58 ± 1.68
Psychological	PVT	50–80	61.83 ± 7.99
	CHF	50–75	63.29 ± 8.31
	Budd chiari	50–100	74.47 ± 15.72
	Cryptogenic cirrhosis	50–80	64.92 ± 9.12
Emotional	PVT	25–75	51.61 ± 13.71
	CHF	50–100	77.1 ± 13.2
	Budd chiari	75–80	77.13 ± 1.85
	Cryptogenic cirrhosis	50–100	78.33 ± 14.28
Social	PVT	50–100	74.47 ± 14.53
	CHF	25–75	55.1 ± 14.6
	Budd chiari	50–80	64.13 ± 8.47
	Cryptogenic cirrhosis	75–100	85.25 ± 8.98
School function	PVT	25–75	47.42 ± 13.19
	CHF	25–75	52.38 ± 13.79
	Budd chiari	25–75	49.13 ± 15.58
	Cryptogenic cirrhosis	25–75	48.08 ± 16.72

Table 4. Individual pediatric quality of life in different etiologies of PHT groups.

QOL score	Hypersplenism absent, n=67	Hypersplenism present, n=24	P
Total	90 (56–100)	73.7 (53–95)	0.001
Physical	90 (38–100)	80 (30–100)	0.001
Psychosocial	87.5 (60–100)	75 (55–95)	<0.001
Emotional	90 (45–100)	85 (50–100)	0.01
Social	95 (50–100)	85 (60–100)	0.003
School functioning	85 (20–100)	70 (25–100)	0.003

Table 5. Pediatric quality of life inventory scores of children (n: 91) with and without hypersplenism. Values are expressed as median (range). QOL ¼ Quality Of Life.

Discussion

The present study summarizes our experience of PHT in children attending the hepatology clinic from 2016 to 2019. The study included 91 patients; their mean age was 5.55 ± 4.30 years. More than 70% of patients were males and from rural areas. Nearly matching with our results, El-Karaksy et al. reported the age of presentation ranged from 1 month to 12 years; 101 out of 169 were boys [9]. It was noted that Portal vein obstruction 39.6% is the commonest cause of portal hypertension at all. followed by CHF 23.1% and 16.5% had Budd Chiari, these results were in concordance to the results of Khanna et al. reported that although EHPVO is relatively

uncommon in Western countries, it is a significant cause of pediatric portal hypertension in the developing world (54% of cases) and accounts for most pediatric upper gastrointestinal bleeding 68%-84% [6].

Also, this was in line with another study to evaluate the etiology of portal hypertension in children admitted in a tertiary care center of Bangladesh on 40 consecutive cases of portal hypertension enrolled from April 2014 to March 2015. This study was conducted by Mahmud et al. reported that 32 (80%) out of 40 children developed portal hypertension because of pre-hepatic causes and 8 (20%) because of hepatic causes. Of 32 children, portal vein obstruction was found in 20 (62.5%) cases in pre-hepatic causes of portal hypertension, splenic vein thrombosis was idiopathic in 4 (12.5%) and 8 (25%) [10]. On the other hand, Grimaldi et al. have reported that the main causes of portal hypertension in children are cirrhosis and congenital hepatic fibrosis [11].

Also, Bernard et al. have reported that cirrhosis was responsible for 51% of portal hypertension cases and extra-hepatic portal venous obstruction was found in 34% of cases [12]. The difference of the current study from other studies as to regard the etiology could be attributed to differences in the living conditions, low socioeconomic, standards of hygiene, and perinatal care which lead to umbilical sepsis, ethnicity, reporting bias as well as diagnostic criteria utilized. This explanation was in line with other studies conducted by Sarin et al. and Omanwar et al. which reported rarity of the PV obstruction in the west, a declining trend with improved standards of living and hygienic conditions support the role of infections, at an early age in the disease pathogenesis [13,14]. In the current study, the patients with the diagnosis of PV obstruction were presented at an earlier age than patients with other etiologies like CHF, Budd Chiari syndrome, or cryptogenic cirrhosis. These results are in agreement with Imanieh et al. reported that EHPVO can present as early as 6 weeks [15].

As observed in the present study, splenomegaly, abdominal distention, and bleeding were the main clinical presentation of patients suffering from PHT. As regarded the clinical signs of PHT, it was found that all cases of PHT had splenomegaly. These results are in agreement with El-Karaksy et al. reported that splenomegaly was present in 87% and hematemesis was a presenting symptom in 58% [9]. Sarin et al., Banerjee et al. and Mitra et al., reported that splenomegaly is present in all cases of PHT [16-18]. Contradictory to our results, other descriptive studies of 55 children and adolescents' cases by Ferri et al. in the pediatric hepatology clinic of the clinical hospital showed that the clinical manifestation of splenomegaly was found in 36.4% of cases [19]. The differences between the results may be attributed to the most studies discussed are stressing on the PV obstruction only and the variation in the number of studied patients. The complications of PHT were developed in ninety percent of our cases. Varices were the major complication of PHT which occurred in 90.1% of the patients, followed by pancytopenia with splenomegaly in 60.4%. These results are in agreement with the majority of the other studies performed by Banerjee et al. [17] Mileti et al. reported that the most important complication of PHT is variceal bleeding [20]. Also, Duché et al. and Lykavieris et al. reported that up to 70% of children with biliary atresia or portal vein thrombosis have esophageal varices, while Bajaj et al. found that Hypersplenism leading to thrombocytopenia was detected in 61.8% of patients [21-23].

In the current study, the history of patients suffering from PHT revealed that: 48.4% of patients admitted to NICU, 72% of them were diagnosed with PV obstruction versus 20% were diagnosed as CHF. NICU admission may be a risk factor to acquire PV obstruction, although, in this study, there was a shortage of data about neonatal events except in 9 patients and, so comparison with other studies was difficult.

Lots of studies as Abd El-Hamid et al., Morag et al. and Weiss et al. reported that Neonatal events, including umbilical catheterization and sepsis, were possible causes of EHPVO in a small number of patients [24-26]. It was observed that liver functions were preserved in patients with PV obstruction while, in patients with cirrhosis there were elevated liver functions, prolongation of PT, and low albumin level. Matching with the current study Chawla et al. reported that in PV obstruction the liver function is normal or near-normal except if PV obstruction occurs in a patient with cirrhosis [27]. In patients with PV obstruction who have ascites, the liver function tests are reported to be slightly abnormal as showed by Rangari et al. in their study about Hepatic dysfunction in patients with extrahepatic portal venous obstruction [28]. Costaguta and Alvarez reported that patients with congenital hepatic fibrosis characteristically have a well-preserved liver function; they behave like those with portal vein obstruction regarding the risk and tolerance to bleeding [29].

In the present study, upper GIT endoscopy was done on 85 patients. More than 90.1% had varices (82 cases). Matching with our results, Ferri et al. in their study reported that 84.9% of the evaluated patients with the endoscopic procedure had esophageal varices [19]. Through this work, propranolol was used in 89 cases while endoscopic band ligation was done in 44 cases and both sclerotherapy and band ligation was done in 14 cases. In agreement with these findings, Gürakan et al. reported that propranolol for prophylaxis of variceal bleeding and sclerotherapy might be the preferred modalities in their study [30]. In contrast, Theocharidou et al. reported that treatment includes pharmacologic, endoscopic, and surgical modalities [31]. Because of their unproven effectiveness and severe adverse effects, β-Adrenergic blockers are not commonly used in children. In the treatment of acute variceal bleeding and varicose eradication, endoscopic approaches such as sclerotherapy and Endoscopic Variceal Ligation (EVL) are highly efficient. There was noted that QOL scores, total and individual domains, that is physical, psychological, emotional, social, and school functioning were significantly lower in all our PHT children, moreover, patients with hypersplenism had lower median total QOL scores in all individual domains than patients without hypersplenism. Hypersplenism is known to develop in the presence of splenomegaly. These results were in concordance to the results of Krishna et al. 32 reported that patients with hypersplenism had lower median total QOL

scores in all individual domains than patients without hypersplenism [32].

Conclusion

From this observational study, we concluded that PHT affects the quality of life of Egyptian children. The most common cause of PHT in children and adolescents was PV obstruction. Splenomegaly was the commonest presentation of PHT, and esophageal varices were the commonest complication.

Limitation of the study

This study has some limitations. Firstly, the present study was a hospital-based cross-sectional study that included only participants from one centre. Therefore, it may not represent the actual scenario of the community epidemiological variables. Secondly, the source of some data as family history and NICU admission in this study was collected from the child's parents which, can lead to a recall bias and limits the number of variables that the study can analyses reliably.

Abbreviations

PHT: Portal Hypertension; PV: Portal Vein; QOL: Quality of Life; HRQOL: Health Related Quality of Life; EHPVO: Extra Hepatic Portal Vein Obstruction; CHF: Congenital Hepatic Fibrosis; PHG: Portal Hypertensive Gastropathy; NICU: Neonatal Intensive Care Unit; EVL: Endoscopic Variceal Ligation; CBC: Complete Blood Count; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase.

Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authors' Contributions

LE designed and directed the study. AA, RA, and MF conducted the study and analyzed the data. LE, AA, RA wrote the manuscript. All authors have read and approved the manuscript.

References

1. Sureka B, Patidar Y, Bansal K, et al. Portal vein variations in 1000 patients: Surgical and radiological importance. Br J Radiol 2015; 88(1055): 20150326.
2. Shneider BL, Bosch J, Franchis de R, et al. Portal hypertension in children: Expert pediatric opinion on the report of the bavenov consensus workshop on methodology of diagnosis and therapy in portal hypertension. Pediatr Transplant 2012; 16(5): 426-437.
3. Merli M, Nicolini G, Angeloni S, et al. Incidence and natural history of small esophageal varices in cirrhotic patients. J Hepatol 2003; 38(3): 266-272.
4. Bosch J, Abraldes JG, Groszmann R. Current management of portal hypertension. J Hepatol 2003; 38 Suppl1: S54-S68.
5. Gonçalves ME, Cardoso SR, Maksoud JG. Prophylactic sclerotherapy in children with esophageal varices: Long-term results of a controlled prospective randomized trial. J Pediatr Surg 2000 ;35(3): 401-405.
6. Khanna R, Sarin SK. Non-cirrhotic portal hypertension-diagnosis and management. J Hepatol 2014; 60(2): 421-441.
7. Varni JW, Seid M, Rode CA. The PedsQL: Measurement model for the pediatric quality of life inventory. Med Care 1999; 37(2): 126-139.
8. http://www.mapi-research-inst.com/lvprocess.asp
9. El-Karaksy HM, El-Koofy N, Mohsen N, et al. Extrahepatic portal vein obstruction in Egyptian children. J Pediatr Gastroenterol Nutr 2015; 60(1): 105-109.
10. Mahmud S, Ahmed SS, Gulshan J, et al. Etiology of portal hypertension in children-an experience in a tertiary centre of Bangladesh. Bangladesh J Child Health 2015; 39(1): 14-7.
11. Grimaldi C, de Ville de Goyet J, Nobili V. Portal hypertension in children. Clin Res Hepatol Gastroenterol 2012; 36: 260–1.
12. Bernard O, Alvarez F, Brunelle F, et al. Portal hypertension in children. Clin Gastroenterol 1985; 14(1): 33-55
13. Sarin SK, Kumar A. Noncirrhotic portal hypertension. Clin Liver Dis 2006; 10(3): 627-x.
14. Omanwar S, Rizvi MR, Kathayat R, et al. A rabbit model of non-cirrhotic portal hypertension by repeated injections of *E. coli* through indwelling cannulation of the gastrosplenic vein. Hepatobiliary Pancreat Dis Int 2004; 3(3): 417-422.
15. Imanieh MH, Dehghani SM, Khoshkhui M, et al. Etiology of portal hypertension in children: A single center's experiences. Middle East J Dig Dis 2012;4(4): 206-210.
16. Sarin SK, Agarwal SR. Extrahepatic portal vein obstruction. Semin Liver Dis 2002; 22(1): 43-58.
17. Banerjee JK. Portal hypertension. Med J Armed Forces India 2012; 68(3): 276-279.
18. Mitra SK, Kumar V, Datta DV, et al. Extrahepatic portal hypertension: A review of 70 cases. J Pediatr Surg 1978; 13(1): 51-57.
19. Ferri PM, Ferreira AR, Fagundes ED, et al. Portal vein thrombosis in children and adolescents: 20 years' experience of a pediatric hepatology reference center. Arq Gastroenterol 2012; 49(1): 69-76.
20. Mileti E, Rosenthal P. Management of portal hypertension in children. Curr Gastroenterol Rep 2011; 13(1): 10-6.
21. Duché M, Ducot B, Tournay E, et al. Prognostic value of endoscopy in children with biliary atresia at risk for early development of varices and bleeding. Gastroenterology 2010; 139(6): 1952-1960.
22. Lykavieris P, Gauthier F, Hadchouel P, et al. Risk of gastrointestinal bleeding during adolescence and early

adulthood in children with portal vein obstruction. J Pediatr 2000; 136: 805–8.

23. Bajaj JS, Bhattacharjee J, Sarin SK. Coagulation profile and platelet function in patients with extrahepatic portal vein obstruction and noncirrhotic portal fibrosis. J Gastroenterol Hepatol 2001; 16: 641–6.
24. Abd El-Hamid N, Taylor RM, Marinello D, et al. Aetiology and management of extrahepatic portal vein obstruction in children: King's college hospital experience. J Pediatr Gastroenterol Nutr 2008; 47(5): 630-4.
25. Morag I, Epelman M, Daneman A, et al. Portal vein thrombosis in the neonate: Risk factors, course, and outcome. J Pediatr 2006; 148: 735–9.
26. Weiss B, Shteyer E, Vivante A, et al. Etiology and long-term outcome of extrahepatic portal vein obstruction in children. World J Gastroenterol 2010 16(39): 4968-72.
27. Chawla Y, Duseja A, Dhiman RK. Review article: The modern management of portal vein thrombosis. Aliment Pharmacol Ther 2009; 30: 881–94.
28. Rangari M, Gupta R, Jain M, et al. Hepatic dysfunction in patients with extrahepatic portal venous obstruction. Liver Int 2003; 23(6): 434–9.
29. Costaguta A, Alvarez F. Etiology and management of hemorrhagic complications of portal hypertension in children. International J Hepatol 2012; pp: 879163.
30. Gürakan F, Eren M, Koçak N, et al. Extrahepatic portal vein thrombosis in children: Etiology and long-term follow-up. J Clin Gastroenterol 2004; 38: 368-72.
31. Giouleme O, Theocharidou E. Management of portal hypertension in children with portal vein thrombosis. J Pediatr Gastroenterol Nutr 2013; 57(4): 419-25.
32. Krishna YR, Yachha SK, Srivastava A, et al. Quality of life in children managed for extrahepatic portal venous obstruction. J Pediatr Gastroenterol Nutr May 2010; 50(5): 531-6.

*Correspondence to:

Asmaa W Abdelaziz

Department of Pediatrics

Ain Shams University

Cairo

Egypt

Tel: 01009771789

E-mail: dr.asmaa.wafeeq@gmail.com