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Characterization of Acute Hepatitis in Children with Special Reference to Fulminant Hepatic Failure

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Abstract
Background*: Viral hepatitis is a major health problem in developing and developed countries. In India all forms of viral hepatitis are seen in paediatric age group. Acute viral hepatitis (AVH) is an important cause of morbidity and mortality in them. Fulminant hepatic failure is a life-threatening condition characterized by jaundice, encephalopathy and coagulopathy leading to multi organ failure in a patient with no prior history of liver disease. The present study determined the current scenario of various infective causes of hepatitis and assess prognostic factors of acute infective hepatitis and fulminant hepatic failure.*
Materials and Methods*: This was a hospital based prospective observation study. 108children (1-15 years old) fulfilling the case definition of acute infective hepatitis and/or fulminant hepatic failure were included in the study duration of 12 months. In each case, age, sex, clinical presentation & laboratory investigations were collected & analysed.*
Results*: Out of 108 children, 59 were boys & 49 were girls. Etiology was established in 83% cases. Viral infections were found to be the most common cause. Hepatitis A virus was the most common causative agent in 50.9% children followed by Hepatitis E virus (8.2%), Salmonella (7.4%), mixed HAV & HEV (6.5%), dengue virus (6.5%), Hepatitis B virus & plasmodium vivax each (1.9%). Thirty children of acute fulminant hepatic failure admitted in pediatric ICU were studied for etiology and prognostic factors. Female gender, hypoglycemia, raised INR & hyperammonemia, higher encephalopathy grade, and presence of multiorgan failure were found to be significant predictors of mortality.*
Conclusions*: Hepatitis is a major public health problem. It is important to educate the society regarding clinical presentation of disease so that they can seek medical intervention early & can reduce significant mortality associated with it.*
Key Word*: Acute infective hepatitis, Fulminant hepatic failure, Hyperammonemia, Multiorgan failure*

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I. Introduction

Hepatitis is a major public health problem and is endemic throughout the world having inadequate sanitary conditions especially in tropical and developing countries [1]. The clinical spectrum of acute infective hepatitis ranges from entirely subclinical & inapparent infection to rapidly progressive fulminant hepatic failure. Despite the availability of vaccines, prophylactic measures & improved sanitation, it affects millions of children every year [2].In India all forms of viral hepatitis are seen in pediatric age group. Acute viral hepatitis (AVH) is an important cause of morbidity and mortality in them.

The common causes for hepatitis in children are hepatitis A, hepatitis B, hepatitis C, hepatitis D, autoimmune hepatitis and metabolic disorders like Wilson's disease and α-1 antitrypsin deficiency. Autoimmune hepatitis was found to be the commonest cause in the western literature while infections are among the lowest;

the biggest chunk is however idiopathic. The scenario is likely to be different in the tropical and subtropical countries like India because of high prevalence of infection. Childhood hepatitis constitutes a significant population of hospital admissions in India. Worldwide, the overall frequency of pediatric liver disease is 1:8,000. According to a study in U.S, it amounts to almost 15,000 hospital admissions per year [3].Hepatitis A virus (HAV) and Hepatitis E virus (HEV) are predominantly enterically transmitted pathogens and are responsible to cause both sporadic infections and epidemics of acute viral hepatitis (AVH). Hepatitis B virus (HBV) and Hepatitis C virus (HCV) are predominantly spread via parenteral route and are notorious to cause chronic hepatitis, which can lead to grave complications including cirrhosis of liver and hepatocellular carcinoma (HCC).

Fulminant hepatic failure is a complication of viral hepatitis and is one of the leading causes of death in hospitalized children with viral hepatitis in India. The condition is very distressing as it occurs acutely in previously healthy children and progresses rapidly inspite of all modern treatment [4]. In India Fulminant hepatic failure in children is associated with very high mortality rate of 70 to 80%. Most cases in our set up are due to waterborne hepatotropic viruses [5].

II. Material and Methods

It was a hospital based observation study conducted in the Department of Pediatrics, S.P. Medical College & P.B.M. Associated Group of Hospitals, Bikaner (Rajasthan) over a period of one year.

Study Design: Hospital based observational study

Study Location: This was a tertiary teaching hospital based study in Department of Pediatrics S.P. Medical College & P.B.M. Associated Group of Hospitals, Bikaner (Rajasthan)

Study Duration: 12 months from September 2019 to August 2020.

Sample size: 108 patients

Subjects and selection method: During the study period 125 children were admitted with acute infective hepatitis & fulminant hepatic failure. 17 patients were excluded due to past history of liver disease or physical signs of chronic liver disease, expiry within few hours of admission & refusal of consent. The study population includes 108 patients who fulfill the above case criteria of acute infective hepatitis & fulminant hepatic failure after informed written consent from parent/guardian. Prognostic factors of fulminant hepatic failure were studied by dividing the children into two groups according to final outcome: **Group A** comprised of those children who expired while **Group B** comprised of those who improved and were discharged.

Inclusion Criteria:

1. All children (1-15 years old) fulfilling the case definition of acute infective hepatitis & fulminant hepatic failure were included.
2. Those willing to provide written informed consent and comply with protocol requirements.

Exclusion Criteria:

1. All the patients with past history of liver disease or features of chronic liver disease were excluded from the study.
2. Non infective causes of hepatitis like drug exposure, metabolic, hemolytic toxins & patients on anti tubercular treatment were excluded.
3. Patients with associated acute or chronic co-morbid conditions were excluded.
4. Subjects unwilling to give consent for the study.

Procedure methodology

Patients were subjected to hematological and biochemical investigations. All children were tested for viral markers for hepatitis. Investigations for other infections like dengue, malaria and enteric fever were conducted, wherever clinically indicated. All children were monitored for hypoglycemia & those with CNS symptoms like seizures, decreased level of consciousness were admitted to PICU & were managed according to standard ICU protocols. Detailed general physical examination and systemic examination including a detailed neurological examination was carried out. Triage scoring, Glasgow coma scale & encephalopathy grading were recorded at the time of admission. Daily follow-up examination was done. Improvement or deterioration in clinical status was noted and required investigations were repeated to determine the progression of illness.

Statistical analysis

Data thus collected was transferred into Microsoft excel sheet & analysed with the help of frequency tables, percentages & appropriate statistical tests like odds ratio, chi-square test, p-value wherever applicable.

III. Results

During the study period 125 children were admitted with acute infective hepatitis & fulminant hepatic failure. 17 children were excluded due to past history of liver disease or physical signs of chronic liver disease, expiry within few hours of admission & refusal of consent. The study population includes 108 children (59 boys) with a mean age of 7.9 years.Hepatitis A virus was the most common causative agent in 50.9% children followed by Hepatitis E (8.2%), Salmonella (7.4%), mixed HAV+HEV infection (6.5%), dengue virus (6.5%), Hepatitis B virus (1.9%), plasmodium vivax (1.9%), in about 16.7% children causative agent remain unidentified (Fig 1). Out of total 108 children, 30 children developed fulminant hepatic failure. 24 children progressed to hepatic encephalopathy in which 4 children to grade I, 8 children to grade II, 8 children to grade III and 4 children to grade IV. Serum ammonia level was also raised in these children in which 11 children had ammonia level up to 54 mcg/dL, 9 children between 55-110 mcg/dL, 2 children between 111-165 mcg/dL, & 8 children >165 mcg/dL. Mean value of serum ammonia was 104.50±83.30 mcg/dL.

Group A constituted 10 children (33%) that expired and Group B constituted 20 children (67%) that survived and were discharged.Among the epidemiological predictors, (Table 1) female had a significant (p value=0.045) higher mortality rate. Children of 5-10 years age group & belonging to rural areas also had higher mortality rate. Among the various clinical predictors of mortality (Table 2) in fulminant hepatic failure children, higher grade ≥ III of hepatic encephalopathy and multi organ failure (involvement of two or more body system) had statistically significant (p value<0.05) higher mortality rate as compared to other. In children who had bleeding manifestation & seizures are also associated with high mortality but result was not found to be statistically significant. Children in whom the interval between onset of prodromal symptoms and onset of encephalopathy was more than 7 days also had higher mortality rate.Among the various biochemical predictors, (Table 3) hypoglycemia i.e. ≤45 mg/dL, higher INR level > 2 & hyperammonemia i.e. serum ammonia level more 110 mcg/dL was found to be statistically significant (p value<0.05) predictors of mortality. Mortality rate in children with total serum bilirubin level >10 mg/dL, serum albumin ≤3.5 gm/dL& blood pH level >7.45 also was higher although the result was not statistically significant.

ROC curve plotted (Fig 2) shows a serum ammonia level >168 mcg/dL to be predictor of mortality with sensitivity of 70% and specificity of 85% (Area under Curve 0.965; p value <0.001).

IV. Discussion

Since fulminant hepatic failure (FHF) is a potentially fatal condition, estimating the likelihood of spontaneous recovery and identifying patients who cannot be salvaged without liver transplant is necessary. Prognostic factors that predict mortality and need for early liver transplant are required.

Our study results shows that viral hepatitis remains the most common cause of fulminant hepatic failure in india. In our study there is a high prevalence of Hepatitis A which was comparable with the studies of Malathi et al[6] (38.6%), Marcus et al [7] (40.18%), Chau et al[8] (49.3%), pooled Indian data (53%). HAV was the leading cause of Acute Viral Hepatitis in all the studies. A study by Behera et al [9] in eastern part of India also showed highest incidence of HAV infection among children. Various studies in different parts of world including India, Pakistan, Nepal and Bangladesh have repeatedly shown that high rates of faeco-orally transmitted acute viral hepatitis is still a very important illness; with prevalence of HAV (3.1-67%) and that of HEV (16.3-66.3 %) in children [10-14]. Combined HAV+HEV infection were present in 6.5% children in our study. The incidence of combined HAV+HEV infection in the studies of Malathi et al[6] was 13.4%, pooled Indian data was 11.17%. Typhoid fever was found to be the third most important cause of hepatitis with the incidence of 7.4%. In the literature, it has been mentioned that typhoid hepatitis is an important cause of morbidity in patient with typhoid fever. Typhoid hepatitis is often mild to moderate nature with abnormal liver function tests.

Female sex had a statistically significant higher mortality rate (58%) in comparison to those of male which was also comparable to the study by Kaur et al [15], in which mortality among female children was found to be 54%. In our study higher grade hepatic encephalopathy (≥III) had statistically significant higher mortality rate of 75% as compared to lower grades. This was comparable with the study by Latif et al [16] in which mortality rate was 85.7% among grade III and 100% among grade IV as these stages are commonly associated with cerebral edema. Other studies also reported higher mortality in higher grade of encephalopathy such as Bendre et al[17] who showed that 12 out of 14 children with grade III and IV encephalopathy expired. We also found that children in whom hypoglycemia (≤45 mg/dL) was present had a statistically significant higher mortality rate of 100% as compared to other children. Srivastava et al [18] proposed that hypoglycemia (blood glucose < 45mg/dL) predicts mortality. It highlights the fact that early detection and appropriate treatment of this potentially treatable complication can improve the outcome. In our study children who presented with INR >2.0 had higher mortality rate as compared to children with INR ≤ 2.0. Aziz et al [19] and Latif et al [16] also showed higher mortality with INR >2. Children in whom serum ammonia level >110 mcg/dl had higher mortality as compared to those with serum ammonia level up to 110 mcg/dl. Pankhaniya et al [20] also reported

higher mortality rate of 100% among children with raised serum ammonia level more than or up to 3 times elevated.

We were able to establish etiology in larger number of patients as compared to previous studies. Our results were different from developed countries that showed that viral hepatitis account for < 10% cases of ALF but are consistent with previous Indian studies that showed that viral hepatitis is the most common cause of mortality. It highlights that the burden of fulminant hepatic failure can be decreased by decreasing viral hepatitis prevalence. As present study is a single centre, small sample size hospital based observation study. Therefore multicentric, large sample size and longer duration community based study is needed to achieve more precise estimation and to improve external validity.

V. Conclusion

From the present study we conclude that hepatitis is a major public health problem. Hepatitis A virus is the commonest causative agent of acute infective hepatitis & fulminant hepatic failure. Female gender, hypoglycemia, raised INR & hyperammonemia, higher encephalopathy grade, and presence of multi organ failure were found to have a direct correlation with the mortality. Good hygiene practices & early immunization could be a step towards prevention of Hepatitis A infection. It is also important to educate the society regarding clinical presentation of disease so that they can seek medical intervention early and can reduce significant mortality associated with it.

References

[1]. Dientardt F. Seroepidemiological study of hepatitis B. WHO Chr. 1983;37(6):203-4.
[2]. Sarker NR, Saha SK, Ghosh DK, Adhikary A, Mridha A, et al. (2014) Seropositivity of viral markers in icteric children. Bangladesh Med J43(1): 26-29.
[3]. Kim WR, Brown RS Jr, Terrault NA, El-Serag H. Burden of liver diseases in the United States: Summary of workshop. Hepatology. 2002;36(1):227-42.
[4]. Anderson D, Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, Harrison's Principles of Internal Medicine, McGraw Hill Medical Publishing Division 16th edition.2015. 285:1822-1832.
[5]. Singh M. Medical emergencies in children. Sagar Publications; 3rd edition. 2000:25;386-406.
[6]. Malathi S, Mohanavalli B. Clinical viral marker pattern of acute sporadic hepatitis in children in Madras, South India. J Trop Pediatr. 1998;45(5):275-8.
[7]. Marcus S, AL-Moslin M. Urological and immunological studies in patients with acute viral hepatitis. Scand J. Immunol. 1993;37:265.
[8]. Chau TN. Acute viral hepatitis in Hong Kong: a study of recent incidences. Hong Kong Med J. 1997;3:261-6.
[9]. Behera MR, Patnaik L. Clinico-biochemical profile and etiology of acute viral hepatitis in hospitalized children: a study from Eastern India. Indian J Child Health. 2016;3(4):317-20.
[10]. Bosan A, Qureshi H, Bile KM, Ahmed I, Hafiz R (2010) A review of hepatitis viral infectionsin Pakistan. J Pak Med Assoc 60(12): 1045- 1054.
[11]. Jain P, Prakash S, Gupta S, Singh KP, Shrivastava S, et al. (2013) Prevalence of hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis D virusand hepatitis E virus as causes of acute viral hepatitis in North India: A hospital based study. Indian J Med Microbiol 31(3): 261-265.
[12]. Irshad M, Singh S, Ansari MA, Joshi YK (2010) Viral hepatitis in India: A Report from Delhi. Glob J Health Sci 2: 96-103.
[13]. Jeong SH, Lee HS (2010) Hepatitis A: Clinical manifestation and management. Intervirology 53:15-19.
[14]. Acharya SK, Madan K, Dattagupta S, Panda SK. Viral hepatitis in India. Natl Med J India 2006; 19(4): 203-217.
[15]. Kaur S, Kumar P, Kumar V, Sarin SK, Kumar A. Etiology and prognostic factors of acute liver failure in children. Indian Pediatr. 2013; 50(7):677-9.
[16]. Latif N, Mehmood K. Risk factors for fulminant hepatic failure and their relation with outcome in children. J Pak Med Assoc. 2010; 60(3):175-8.
[17]. Bendre SV, Bavdekar AR, Bhave SA, Pandit AN, Chitambar SD, Arankalle VA. Fulminant hepatic failure-etiology, viral markers and outcome. Indian Pediatrics. 1999;36:1107-12.
[18]. Srivastava A, Yachha SK, Poddar U. Predictors of outcome in children with acute viral hepatitis and coagulopathy. J Viral Hepat. 2012; 19(2):e194-201.
[19]. Aziz S, Muzaffar R, Hafiz S, Abbas Z, Zaar MN, Anwar SA, et al. Helicobacter pylori, hepatitis viruses A, C, E antibodies and HBsAg prevalence and associated risk factor in paediatric communities of Karachi. J Coll Physician Surg Pak 2007; 17: 195-8.
[20]. Pankhaniya RN, Parikh YN, Mohan DS. Study of acute viral hepatitis with special reference to fulminant hepatic failure. Int J ComtempPediatr 2018; 5(4):1533-6.

Fig 1 Distribution of Causative Agents among Acute infective hepatitis children (N=108)

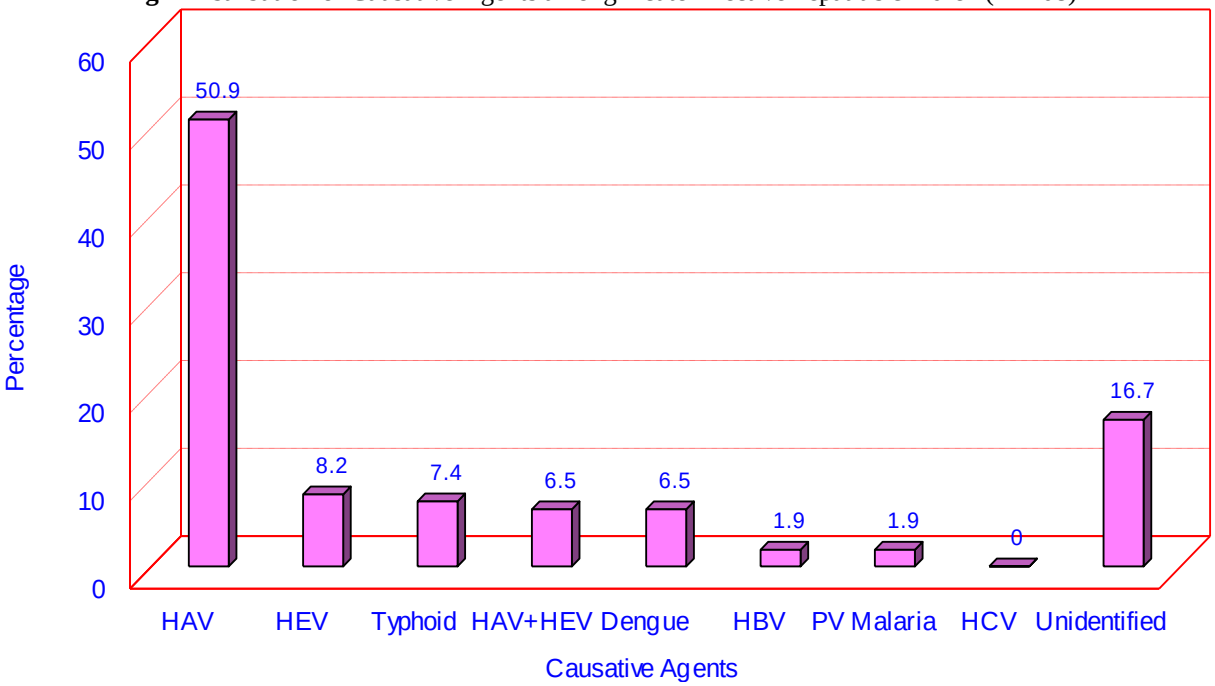


Table 1 Epidemiological predictors of mortality in fulminant hepatic failure children (N=30)

Parameter	Number N=30 (100%)	Group A (death) N=10 (33%)	Group B (discharged) N=20 (67%)	Odds ratio	95% CI	P value
Age Group (years)						
1-5	7(23%)	1/7(14%)	6/7(86%)			
5-10	17(57%)	7/17(41%)	10/17(59%)	2.333	0.465-11.693	0.440
10-15	6(20%)	2/6(33%)	4/6 (67%)			
Gender						
Female	12(40%)	7/12(58%)	5/12(42%)	7.000	1.293-37.909	0.045
Male	18(60%)	3/18(17%)	15/18(83%)			
Residential area						
Rural	21(70%)	8/21(38%)	13/21(62%)	2.154	0.356-13.049	0.675
Urban	9(30%)	2/9(22%)	7/9(78%)			

Table 2 Clinical predictors of mortality in fulminant hepatic failure children (N=30)

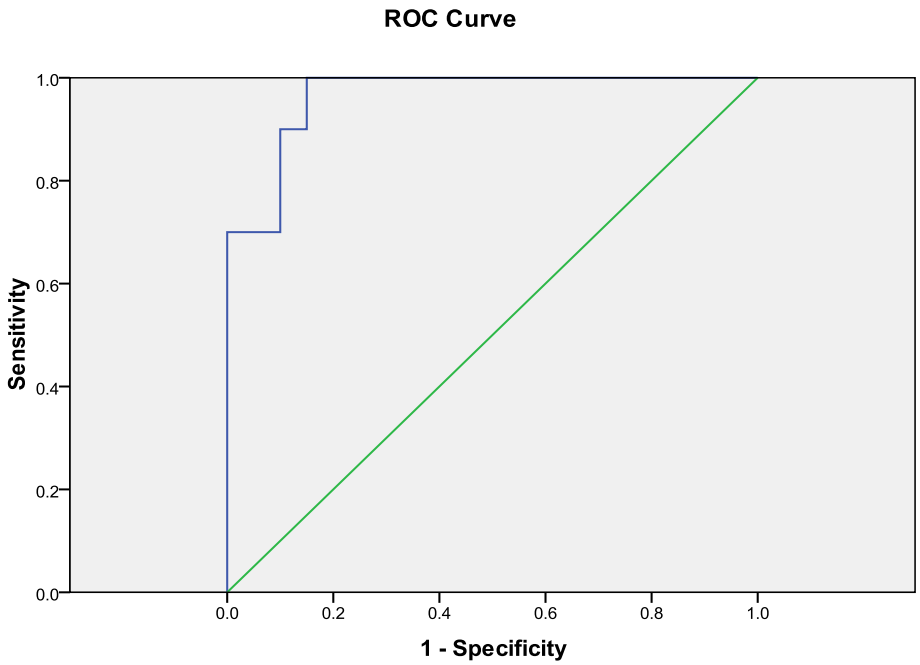
Parameter	Number N=30 (100%)	Group A (death) N=10 (33%)	Group B (discharged) N=20 (67%)	Odds ratio	95% CI	P value
Bleeding						
Yes	11(37%)	5/11(45%)	6/11(55%)	2.333	0.488-11.167	0.425
No	19(63%)	5/19(26%)	14/19(74%)			
Onset of symptoms (days)						
>7 days	4(13%)	2/4(50%)	2/4(50%)	2.250	0.267-18.925	0.584
≤7 days	26(87%)	8/26(31%)	18/26(69%)			
Encephalopathy grade						
≥ III	12(40%)	9/12(75%)	3/12(25%)	51.000	4.612-563.90	<0.001
< III	18(60%)	1/18(6%)	17/18(94%)			
Seizures						
Yes	8(27%)	4/8(50%)	4/8(50%)	2.667	0.500-14.217	0.384
No	22(73%)	6/22(27%)	16/22(73%)			
Multiorgan failure						
Present	12(40%)	7/12(58%)	5/12(42%)	7.000	1.293-37.909	0.045
Absent	18(60%)	3/18(17%)	15/18(83%)			

Table 3 Biochemical predictors of mortality in fulminant hepatic failure children (N=30)

Parameter	Number N=30 (100%)	Group A (death) N=10 (33%)	Group B (discharged) N=20 (67%)	Odds ratio	95% CI	P value
Blood glucose (mg/dL)						
≤45 mg/dl	5(17%)	5/5(100%)	0/5(0%)	-	-	0.002

>45 mg/dl	25(83%)	5/25(20%)	20/25(80%)			
Total Serum Bilirubin (mg/dL)						
>10 mg/dL	5(17%)	2/5(40%)	3/5(60%)	1.417	0.196-10.227	1.000
≤10 mg/dL	25(83%)	8/25(32%)	17/25(68%)			
S. Albumin (gm/dL)						
≤3.5	23(77%)	8/23(35%)	15/23(65%)	1.333	0.209-8.486	1.000
>3.5	7(23%)	2/7(28%)	5/7(72%)			
Blood pH						
>7.45	5(17%)	3/5(60%)	2/5(40%)	3.857	0.527-28.241	0.300
7.35-7.45	18(60%)	5/18(28%)	13/18(72%)			
<7.35	7(23%)	2/7(28%)	5/7(72%)			
INR						
>2.0	6(20%)	5/6(83%)	1/6(17%)	19.000	1.790-201.68	0.009
≤2.0	24(80%)	5/24(21%)	19/24(79%)			
Hyperammonemia (mcg/dL)						
>110	10(33%)	9/10(90%)	1/10(10%)	171.00	9.570-3055.5	<0.001
≤110	20(67%)	1/20(5%)	19/20(95%)			

Fig 2 Receiver Operating Characteristics (ROC) curve for Serum Ammonia level in fulminant hepatic failure children



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