Brain MR imaging and 1H-MR Spectroscopy Changes in Patients with Extra-Hepatic Portal Vein Obstruction from Early Childhood to Adulthood

S. K. Yadav[1], S. Saksena[1], A. Srivastava[2], A. Srivastava[1], V. A. Saraswat[3], M. A. Thomas[4], R. S. Rathore[5], and R. K. Gupta[1]

[1]Radiodiagnosis, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [2]Pediatric gastroenterology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [3]Gastroenterology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [4]Radiological Sciences, UCLA School of Medicine, Los Angeles, CA, Los Angeles, CA, United States, [5]Mathematics and Statistics, Indian Institute of technology Kanpur, Kanpur, Uttar Pradesh, India

Introduction: Extra-hepatic portal vein obstruction (EHPVO) is a condition in which there is mechanical obstruction to portal venous flow. It may be a partial or complete obstruction of the main portal vein with or without obstruction to its tributaries, in the absence of liver cirrhosis or malignancy (1). The quality of life in patients with EHPVO is superior to those with liver cirrhosis since hepatocellular function is normal. Abnormal cognitive functions interfere significantly with the daily functioning and lead to impairment of health related quality of life in patients with liver cirrhosis having (minimal hepatic encephalopathy) MHE (2). It is generally agreed that hepatic encephalopathy occurs due to the effect of toxins on the brain, the most important being ammonia (3). Brain MRI, ^{1}H-MR (^{1}H-MR) Spectroscopy, diffusion and diffusion tensor imaging (DTI), magnetization transfer imaging and F-MRI have been used to understand the pathophysiological alterations in patients with cirrhosis (4) at different age group, however in patients with EHPVO, such information is sparse (5). The aim of this study was to look for the age related changes in brain MRI and metabolite profile on ^{1}H-MR spectroscopy in patients with EHPVO and to explore any correlation of imaging and ^{1}H-MR Spectroscopy parameters with blood-ammonia.

Materials and Methods: Sixty-three patients with EHPVO [children, 7-12 years (n=22), adolescents, 13-18 years (n=15) and adults, 19-41 years (n=26)] and 47 age/sex matched controls were studied. Diagnosis of EHPVO was based on consensus guidelines of Asian Pacific Association for the Study of Liver (6). All patients underwent for blood test, imaging and endoscopy for the assessment of varices. Neuropsychological tests, conventional MRI, diffusion tensor imaging (DTI) ^{1}H-MR Spectroscopy and blood-ammonia estimation were performed in all subjects. DTI and ^{1}H-MR spectroscopy data acquisition and processing are done according to our previous accepted study (7). The study protocol was approved by the institutional ethics committee and written informed consent obtained by each individual. ANOVA post-hoc tests were performed among controls and patients with MHE and no-MHE in all three-age-groups. Pearson's correlation coefficient was used to compute correlation among different parameters.

Results: Of 63 EHPVO patients, 25 (40%) patients had MHE who showed significantly increased mean diffusivity, Glx/Cr, blood-ammonia and globus pallidus T1hyperintensity (GP T1 H) in all three age groups; however, mIns/Cr was significantly lower only in adults when compared to controls (table1, figure 1). Mean diffusivity positively correlated with blood-ammonia and Glx/Cr in all age groups (figure 2). A significant positive correlation was observed between Glx/Cr and blood-ammonia.

Discussion: It is generally accepted that increased blood-ammonia induces brain glutamine synthesis in the astrocytes which results in cognitive impairment in cirrhotic patients. Minguez et al (5) have reported increased blood-ammonia in adult EHPVO patients with minimal encephalopathy. In the current study, blood-ammonia levels progressively increased across controls to no-MHE to MHE in all the three age groups. This may be due to increased extrahepatic collateral vessels, resulting in increased shunting of ammonia directly into the blood from the gut resulting in further impairment in cognitive functions in these patients with advancing age. An increase in mean diffusivity, Glx/Cr, blood-ammonia and GP T1 H and decrease in mIns/Cr is associated with the pathogenesis of MHE in adults with EHPVO. No change of Cho/Cr in EHPVO may serve as a diagnostic marker for its differentiation from cirrhosis induced MHE. However lack of mIns/Cr reduction in pediatric and adolescent group suggests that caution needs to be exercised while interpreting ^{1}H-MR spectroscopy data in pediatric patients with EHPVO. A significant positive correlation of blood ammonia with Glx/Cr support the hypothesis that ammonia is central in the pathogenesis of MHE in EHPVO, A positive correlation of MD with Glx/Cr and ammonia indicates that hyperammonia contributes to the generalized low grade cerebral edema and cognitive decline in these patients.

Table 1: Summary of Mean Blood Ammonia Levels and Metabolite Ratios in Healthy Controls, Patients with MHE and no-MHE in Three Different Age Groups.

Blood Ammonia and metabolites	Healthy control	no-MHE	MHE	p-value
Pediatric age group (Mean ± SD)				
GP T1 H	462.2±24	537.0±82	570.1±25	0.00
Blood Ammonia	41.9±1.5	128.8±25.5	144.7±25.4	0.00
Glx/Cr	2.22±0.38	2.50±0.29	2.66±0.31	0.01
mIns/Cr	0.48±0.12	0.51±0.11	0.49±0.12	0.66
Cho/Cr	0.21±0.02	0.20±0.03	0.23±0.04	0.08
NAA/Cr	1.21±0.25	1.23±0.14	1.24±0.27	0.91
Adolescent age group (Mean± SD)				
GP T1 H	501.8±42.87	550.9±49.15	595.0±71.17	0.00
Blood Ammonia	43.8±1.5	125.2±45.3	130.2±26.4	0.00
Glx/Cr	1.80±0.46	2.54±0.51	2.74±0.46	0.01
mIns/Cr	0.48±0.16	0.49±0.12	0.34±0.06	0.06
Cho/Cr	0.21±0.03	0.24±0.03	0.20±0.05	0.10
NAA/Cr	1.19±0.27	1.24±0.45	1.20±0.42	0.95
Adult age group (Mean ± SD)				
GP T1 H	588.8±42.87	598.9±49.15	661.0±71.17	0.00
Blood Ammonia	44.8±1.5	125.1±43.5	157.7±36.0	0.01
Glx/Cr	2.08±0.53	2.32±0.64	2.60±0.54	0.04
mIns/Cr	0.50±0.16	0.44±0.17	0.35±0.15	0.04
Cho/Cr	0.23±0.03	0.22±0.07	0.21±0.05	0.59
NAA/Cr	1.27±0.18	1.10±0.19	1.12±0.50	0.20

References- (1) Sarin SK et al. Liver International 2006; 26:512-519. (2) Marchesini G et al. Gastroenterology 2001; 120:170-178. (3) Shawcross D. L. et al. Metab Brain Dis 2007; 22:125–138. (4) Miese F et al. Am J Neuroradiol 2006; 27:1019-1026. (5).Minguez B Hepatology 2006;43:707-714. (6) Sarin SK et al. Liver Int 2006;26:512-519. (7) Saksena S et al. J. Gastroenterol Hepatol 2008; 23, 111-119.

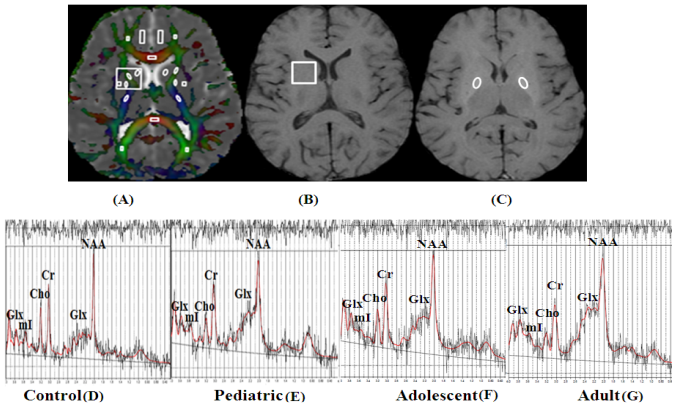

Figure (1) A. axial colour coded FA map fused with MD map showing the ROI(s) placement, (B) for spectroscopy voxel and (C) for T1 quantitation. LC model processed localized 1H-MRS show the metabolite pattern of different age group (E), (F), (G) of patients with adult control (D).

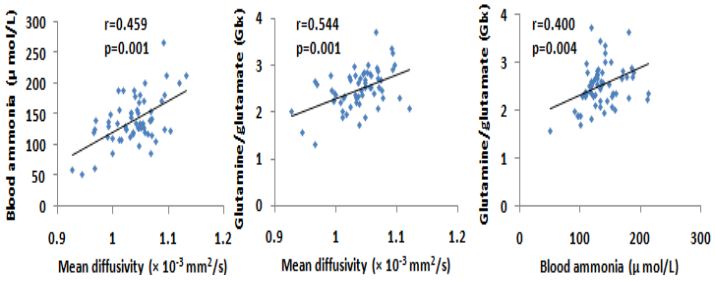

Figure 2. Scatter plots show significant positive correlation of MD values derived from coordinates of spectroscopy with blood-ammonia (A) and Glx (B). Scatter plot (C) shows significant positive correlation between blood-ammonia and Glx in these patients. All age group data of EHPVO patients were pooled together for estimation of correlation.