MINIMAL HEPATIC ENCEPHALOPATHY IN CHILDREN WITH EXTRA HEPATIC PORTAL VEIN OBSTRUCTION

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DM DEGREE IN MEDICAL GASTROENTEROLOGY

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CERTIFICATE

This is to certify that the dissertation entitled **"MINIMAL HEPATIC ENCEPHALOPATHY IN CHILDREN WITH EXTRA HEPATIC PORTAL VEIN OBSTRUCTION"** is a bonafide work done by **Dr. Raja Yogesh K.** at Madras Medical College, Chennai, in partial fulfilment of the university rules and regulations for award of D.M., Degree in Medical Gastroenterology (Branch-IV), under my guidance and supervision during the academic year 2011 -2014.

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DECLARATION

I solemnly declare that this dissertation entitled "**MINIMAL HEPATIC ENCEPHALOPATHY IN CHILDREN WITH EXTRA HEPATIC PORTAL VEIN OBSTRUCTION"** was done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, during 2011-2014, under the guidance and supervision of **Prof. MOHAMMED ALI M.D, D.M.** This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of D.M. Degree in Medical Gastroenterology (Branch-IV).

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INTRODUCTION

Extra-Hepatic Portal Vein Obstruction is one of the vascular disorders of the liver. It is said to occur when there is obstruction to the extra hepatic part of the portal vein with or without the involvement of the intrahepatic part, splenic vein or the superior mesenteric vein. [1] In children, it accounts for nearly 70% of the cases of portal hypertension and is the commonest cause of upper GI bleed in them.[2] In Adults, EHPVO is responsible for nearly one-third of cases of portal hypertension.[3]

Etiologically, EHPVO is a heterogeneous disease and the cause varies with respect to age and geographic location. Umbilical sepsis, umbilical vein catheterisation, intra-abdominal sepsis, congenital malformations of the portal vein, hypercoagulable states, trauma have all been documented as possible etiological factors. [4-7] However, despite the best of efforts, a clear aetiology remains elusive in a vast majority of cases.

Patients with EHPVO can present in two clinical forms: 1) Acute form and 2) Chronic form, with the latter being distinctly more common than the former. In its acute form, patients may present with acute abdominal pain sometimes associated with low grade fever and rarely as transient ascites.

In its more common Chronic form, patients present with variceal bleeding, moderate to massive splenomegaly and features suggestive of hypersplenism. Rarely patients may present with jaundice secondary to portal biliopathy.

Hepatic encephalopathy or porto-systemic encephalopathy refers to the spectrum of neuropsychiatric disturbances seen in patients with liver disease. It ranges from sub-clinical neurological impairment to frank coma. The occurrence of spontaneously occurring overt hepatic encephalopathy is distinctly rare in patients with EHPVO.[8] Minimal Hepatic encephalopathy at one end of the HE spectrum, refers to subtle intellectual deficits and abnormalities in psychomotor performance that is clinically in-apparent but evident on performing specialized psychometric tests.[9-11] Though the occurrence of minimal hepatic encephalopathy has been well documented in patients with cirrhosis, its occurrence in EHPVO, in the absence of inherent liver disease is much less explored. Preliminary studies in adults have suggested the possible existence of MHE.[12-14] The prevalence of MHE in children with EHPVO and its impact when present, have not been studied.

This study aims to evaluate children with EHPVO for the existence of MHE by using Psychometric tests and Critical flicker Frequency. I believe that establishing the presence of MHE in children with EHPVO would lay the foundation for treatment modalities, with the potential to improve scholastic performance and overall intellectual and psychological development of these children.

REVIEW OF LITERATURE

DEFINITION:

According to the Baveno V consensus, EHPVO is defined as the obstruction of the extra-hepatic portion of the portal vein with or without involvement of the intra-hepatic portal branches. [15]

In other words it indicates portal hypertension due to blockade of the portal vein before it enters the liver. The term EHPVO however, does not include isolated thrombosis of splenic vein or superior mesenteric vein.

EHPVO is considered a vascular hepatic disorder. Most of these patients do not have any inherent parenchymal liver disease. Consequently, portal vein obstruction, which can commonly occur in the setting of cirrhosis or hepatocellular carcinoma is generally not considered to be a part of EHPVO. [16]

The term portal vein thrombosis does not exactly reflect the condition of EHPVO as the term "*Portal Vein Thrombosis*" does not exclude the isolated thrombosis of intrahepatic part of the portal vein which occurs in cirrhosis or the invasion of portal vein by hepatocellular carcinoma. Moreover, the term also does not include the development of the portal cavernoma that is pathognomonic of the condition in its chronic form. Hence the term EHPVO has come into acceptance, to denote the distinct

condition in which there is obstruction at the level of the extrahepatic part of the portal vein in an otherwise normal liver.

EPIDEMIOLOGY

EHPVO is one of the commonest causes of Portal Hypertension in the developing world, accounting for 30-55% of all variceal bleeds. It is second to cirrhosis as the cause of portal hypertension (up to 13%) in the West. [17] It is the most common cause of Upper GI bleeding in the paediatric population and accounts for nearly 70% of children with PHT.[2]

INDIAN SCENARIO:

Studies in Indian children have shown that EHPVO is responsible for 54% of portal hypertension. [18] Almost 85-92% of the UGI bleed in Indian children was secondary to portal hypertension due to EHPVO. [17]

Literature from India also suggests that most of these children with EHPVO belong to low and lower-middle socio-economic strata. The increased incidence of neo-natal umbilical sepsis and recurrent gastro-intestinal infections, more common in children of lower socio-economic groups probably explains this epidemiological phenomenon. Over the years it has also been observed that the incidence of EHPVO in children is also steadily declining. This has led to the plausible hypothesis that the

aetiology might have be related to the standard of living and that with improvement in living conditions, the incidence is likely to fall further.

ETIOPATHOGENESIS

The etiopathogenesis in EHPVO has not been well elucidated. The theories put forward are quite heterogeneous and not well supported by hard evidence. Some of the aetiologies suspected are as follows.

1. INFECTIONS

Neo-natal umbilical sepsis, omphalitis, intra-abdominal sepsis either overt or occult have all been alleged to cause EHPVO in children.[19] Neonatal umbilical vein catheterisation done for intravenous infusions and exchange transfusions has also been implicated as a possible etiological factor. Abdominal sepsis has also been postulated as a causative factor in adults.

2. CONGENITAL ANOMALIES

Congenital anomalies of the left and right vitelline veins, from which the portal vein is derived are also hypothesized as a causative factor.[20]

3. PROTHROMBOTIC STATES

Prothrombotic states have been reported to be the underlying factor in a small fraction of cases in children.[21,22] In adults, an underlying prothrombotic state is more commonly found than in children with EHPVO. Underlying latent myeloproliferative disorders and the use of oral contraceptive pills have also been implicated in adults with EHPVO.

4. ABDOMINAL TRAUMA AND SURGERY

Abdominal trauma and surgery has also been alleged to be a cause of EHPVO in a small proportion of cases.

5. IDIOPATHIC

There is no discernible aetiology in a large proportion of cases of EHPVO, especially in the paediatric age group. In Indian children the proportion of idiopathic EHPVO is as high as 90%. [24]

PATHOLOGY

Most commonly the entire length of the portal vein is obstructed by the thrombus. In Indian children, it is observed that the most common site of obstruction is at the portal vein formation[39%], followed by the entire length of portal vein [34%], splenic vein [16%] and the entire spleno-renal axis [11%].

THE PORTAL CAVERNOMA:

The portal cavernoma is the pathognomonic feature of chronic EHPVO. The portal vein is grossly replaced by a sheath of variably sized tortuous channels in a connective tissue matrix. This is called as the portal cavernoma. It is formed by the porto-portal collaterals that develop within the thrombosed part of the portal vein. The perfusion to the liver is hence not as severely compromised as would be expected otherwise. The development of porto-systemic collaterals occurs over time leading to the formation of varices at various sites in the GI tract.

Liver function is usually preserved and most often the histology reveals a normal architecture. Alterations in the liver storage function and transport maximum for bromsulphalin and abnormalities in liodocaine excretion have been documented. Liver biopsy is usually not indicated in clear cut cases of EHPVO.

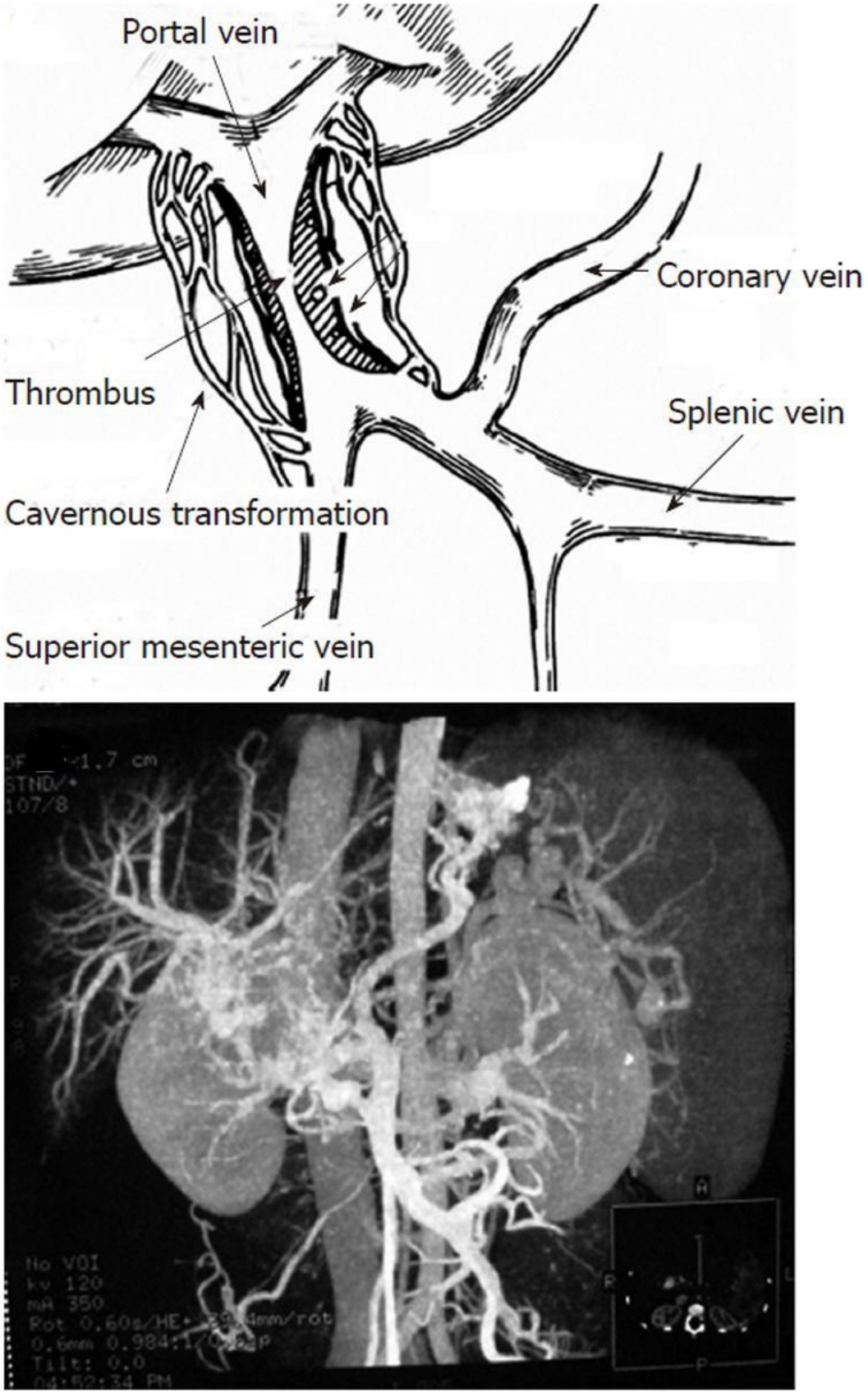


Figure1: Portal Cavernoma

CLINICAL FEATURES

EHPVO has two clinical forms; namely **Acute** or recent EHPVO and the more common **Chronic** form.

ACUTE EHPVO

Most often, the acute form goes unnoticed. Sometimes, there is transient abdominal pain, fever or rarely ascites. There is no portal cavernoma formation on imaging and there is absence of varices.

CHRONIC EHPVO

The more common of the two forms, the usual clinical presentation is with an episode of variceal bleed. Massive splenomegaly, with or without features of hypersplenism is also a common mode of presentation.

VARICEAL BLEEDING

Most children present with an episode of variceal bleeding.[25] Often it is a massive episode and occurs commonly in the first or second decade. Most often the site of bleeding is from oesophageal varices. The bleeds are usually well tolerated. There are no features suggestive of hepatic

decompensation during these episodes. Gastric varices are often seen in about 70% of cases. Most of these varices are gastro-oesophageal varices than isolated gastric varices.[26-28] The propensity for these gastric varices to bleed increases significantly after eradication of oesophageal varices.

Rectal varices are also not uncommon. It is as common as 34-64%.[29] The incidence is probably related to the duration and location of obstruction. The incidence of rectal varices also increases after oesophageal varices are obliterated by endotherapy.

The risk of varices to bleed depends on their size. Larger varices have a greater propensity to bleed. [30] Other determinants are the vessel wall thickness and the supporting tissue. But these parameters are more difficult to assess. The precipitating factors alleged are reflux oesophagitis, NSAID intake and fever. [31]

ABDOMINAL MASS

Abdominal mass is the presenting feature in nearly 10% of children.[32] Usually the splenomegaly is massive and may enlarge to extend even up to the right iliac fossa. Massive splenomegaly can result in hypersplenism manifesting as anaemia and thrombocytopenia

ABDOMINAL PAIN

Pain most often is in the form of a dull ache secondary to the massive splenomegaly. Rarely splenic infarction or extension of the venous thrombosis may be the cause.[33]

ASCITES

Ascites occurs in a small proportion of children following variceal bleeding and is most often transient.[34] Very rarely children develop intractable ascites and these children may benefit from paracentesis or shunt surgery.

ECTOPIC VARICES

Ectopic varices are not uncommon and can occur in around 27-40%.[16] Varices in the duodenum, gall bladder bed and anorectal region are the most common sites of ectopic varices .

JAUNDICE

Rarely jaundice may be the presenting feature of EHPVO. This occurs as a result of portal biliopathy. Portal biliopathy is the term given to abnormalities of extra hepatic and intrahepatic biliary apparatus that occurs as a consequence of portal hypertension. They may result from

compression by the paracholedochal collaterals on the bile ducts and result in narrowing, strictures, angulations and irregularities of the bile ducts. Though features suggestive of portal biliopathy has been demonstrated in as high as 80-100% in adults with EHPVO, these changes are less common in children.[35]

HYPERSPLENISM:

Sequestration of blood cells in the spleen and premature destruction can manifest as pancytopenia. Rarely a sequestration crisis can occur, resulting in hypovolemia and shock.

GROWTH RETARDATION

Children with EHPVO often suffer from growth retardation.[36, 37] Various mechanisms have been put forward to explain the reasons behind growth retardation. Poor absorption related to portal hypertensive enteropathy, impaired synthesis of growth factors like IGF 1 and IGFBP-3 due to shunting of blood away from the liver, recurrent GI bleeds & infections result in growth impairment. [38] Mesenterico-left portal vein shunts which by-pass the site of obstruction and return the portal venous blood to the liver have been shown to result in improvement in growth

parameters, whereas endotherapy has not been shown to affect the growth trend positively. [39, 40]

COGNITIVE AND PSYCHOMOTOR DEFICITS

Overt hepatic encephalopathy is very rare in the setting of EHPVO, when the underlying hepatic function is normal. [41] Minimal cognitive deficits and psychomotor dysfunction has been reported in patients with EHPVO.[14,13,42] The proposed mechanism behind the neurological dysfunction is the shunting of the portal blood away from the liver due to the presence of porto-systemic collaterals; thereby compromising the detoxifying function of the liver. This is an example of TYPE B hepatic encephalopathy – [Hepatic encephalopathy associated with porto-systemic shunting in the absence of intrinsic hepato-cellular disease].[43] Neuro-psychological testing in ten patients with portal vein thrombosis revealed abnormalities in five patients according to a study done by Minguez B et al.[42] Indian studies done in adult EHPVO patients have also shown that MHE is prevalent in these patients. [44, 12] In a study by S.K. Yadav et al, changes in MRI and Magnetic Resonance Spectroscopy consistent with MHE were found in a population of EHPVO that included children, adolescents and adults.[45] The diagnosis of MHE remains a challenge in

children with EHPVO since there is a lack of standardisation in the psychometric tests that are conventionally employed in detecting MHE.

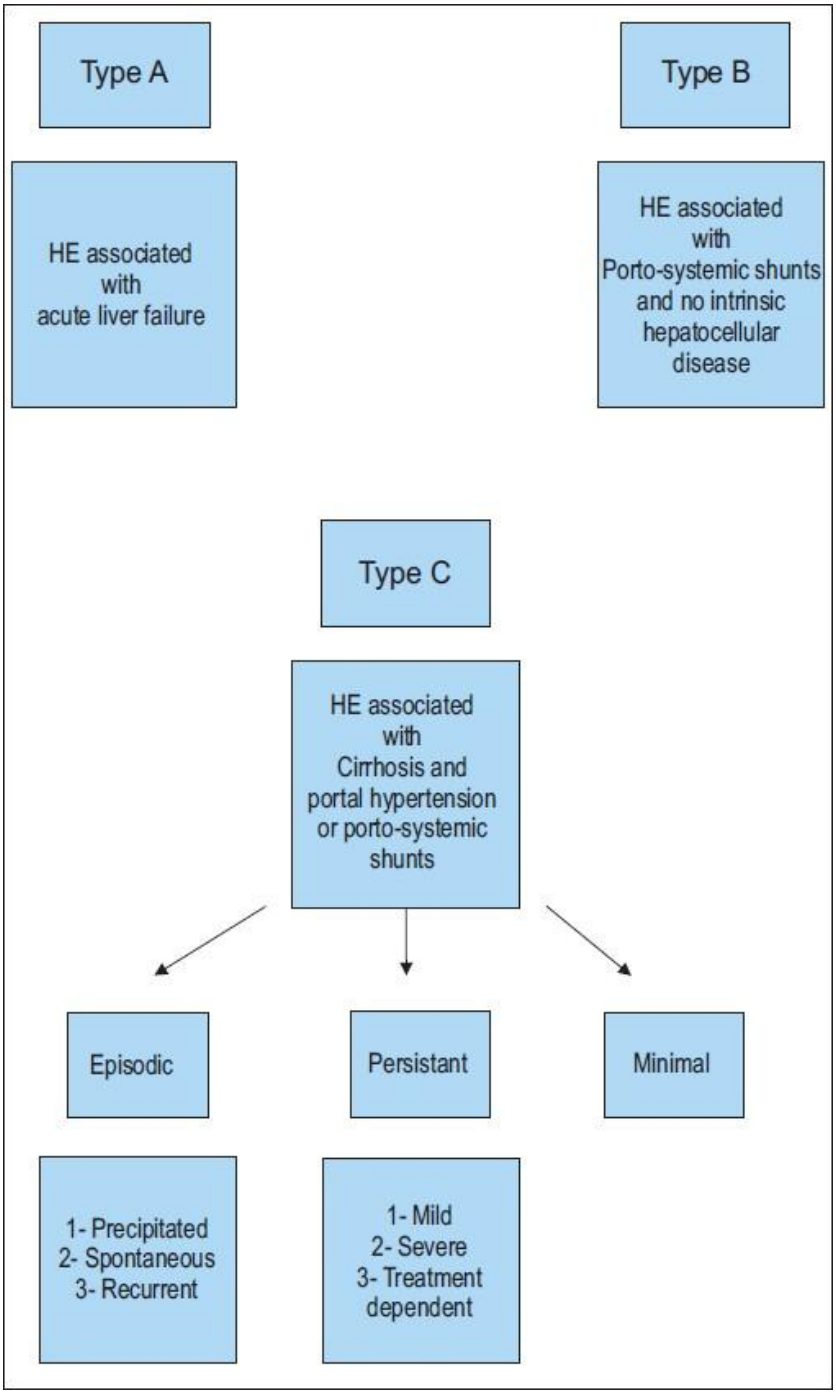


Figure 2: Classification of Hepatic Encephalopathy according to 11th World Congress of Gastroenterology, Vienna 1998

MINIMAL HEPATIC ENCEPHALOPATHY

Minimal Hepatic Encephalopathy is the mildest form in the wide spectrum of hepatic encephalopathy. Patients with Minimal Hepatic Encephalopathy have a normal mental and neurological status on routine clinical examination but demonstrate a variety of deficits neuropsychiatric and neuro-physiological deficits on specialized testing.

It was previously termed as '*Sub-Clinical Hepatic Encephalopathy*', but it was recommended by the World Congress of Gastroenterology that the term *"Minimal Hepatic Encephalopathy"* is a better descriptive terminology, since the term 'Sub-clinical' may be misinterpreted to signify a lack of clinical importance. [45]

Although termed 'minimal', the impact of MHE can have a far greater impact on daily life activities. In patients with cirrhosis, it was shown that MHE was an independent factor in decreasing the quality of life, even after adjusting for the Child- Pugh status. [46] MHE is characterized by a delayed reaction time and an abnormal response inhibition.[47,48] The practical implications of these impediments are many. Impairment in driving skills of patients with MHE has been shown to exist in various studies. [49-52]

Patents with MHE were also impaired when it came to activities like social interaction, sleep, work, home-management and recreational activities when compared to controls. [53, 54] Disturbances in memory are a common feature in MHE. [55] The working or short term memory is characteristically affected while the long term memory is usually intact.

PATHOGENESIS OF MHE

The postulated pathogenesis of MHE is on the same lines as overt hepatic encephalopathy. Moreover, it has been shown that many patients with MHE eventually go on to develop overt HE, and that patients with MHE have nearly four times the risk of developing overt HE than those without.[56]. This underlines the common pathogenic mechanisms underlying the spectrum of Hepatic Encephalopathy. Nitrogenous substances which are derived from the gut are thought to play a major role in the pathogenesis of MHE. Ammonia levels are significantly elevated in patients with HE. Ammonia has been shown to alter cerebral perfusion and decrease glucose utilisation in different cortical sites. This has been shown to correlate well with the decline in cognitive function. [57, 58] Alterations in the glio-neuronal communications lead to astrocyte swelling. These changes seen in overt HE are also seen in MHE. Alterations in the

homeostasis of Manganese have also been suggested as one of the pathogenic mechanisms. [59, 60]

DIAGNOSING MHE

MHE by definition requires that the patient is normal on routine clinical examination. MHE is characterised by subtle disturbances in intellectual and psycho-motor function that is made out only by special tests. The tests can be broadly divided into *Neuro-psychological tests*, *Neurophysiological tests*, *Computerized tests* and *MR imaging & Spectroscopy*.

NEURO-PSYCOLOGICAL TESTING

These tests are simple clinical tests of cognitive function and require no specialised equipment. They are perhaps the most widely established and trusted tests to ascertain cognitive impairment. Most tests are paper and pencil tests that can be carried out at the bed-side. These tests require attention, visuo-spacial orientation and fine motor skills – faculties which are most affected in MHE.

The most common tests employed are Number Connection Tests A and B, the Figure connection Tests, Block Design tests and Digit Symbol tests. These tests are usually compared with the normative data of age and

education matched normal population. Other tests which have been tried are the WAIS - Wechsler Adult Intelligence Scale (WAIS) for verbal and performance skills, Clinical Hepatic Encephalopathy Staging scale- CHESS, Mini Mental Status Examination etc.

THE PYCHOMETRIC HEPATIC ENCEPHALOPATHY SCORE

This is a standardized test battery which is more specific and sensitive for diagnosing MHE. This consists of two trail making tests, namely Number connection Tests-A, Number Connection Tests-B, Serial Dotting Test, Digit Symbol Tests and Line tracing test. Using the combination of tests has increased the accuracy in detecting MHE. Each test result is said to be abnormal if it varies by greater than 2 standard deviations from matched normative data. MHE is diagnosed if two or more tests are abnormal in this battery. Motor speed and accuracy, visuo-spatial orientation, visual perception, visual construction, attention, concentration, and memory, which are commonly challenged in patients with MHE, are tested in PHES.

NEURO-PHYSIOLOGICAL TESTS:

These include Electro-encephalogram, Evoked potential testing, and Critical Flicker Frequency. The EEG changes and evoked responses are less specific and sensitive for diagnosing MHE. The Evoked potential testing can be of two types namely –Exogenous evoked potentials and Endogenous evoked potentials. Among these the P300 peak obtained in an auditory oddball paradigm is said to have a higher sensitivity in detecting MHE. [61] These tests supplement psychometric tests and can be used in combination. The disadvantage of these tests is that they require specialized equipment and cannot be carried out in the out-patient department.

CRITICAL FLICKER FREQUENCT TESTING

This is a type of neuro-physiological tests that is based on determining the threshold below which a flickering light source is appreciated as a continuous one. Visual discrimination ability and general arousal are the faculties tested in this test. Many clinical studies have proven its usefulness in detecting MHE.[62-63] The test is simple and accurate with a high reproducibility. It also said to be less dependent on age, education and training

INHIBITORY CONTROL TEST

This is a computerized test measuring the attention span and response inhibition. It has been used in testing of various psychiatric conditions and has also been found to be sensitive for diagnosis and follow up of MHE

MAGENETIC RESONANCE IMAGING AND SPECTROSCOPY

Changes in the form of hyper-intense signals in T1 weighted images of the globus pallidus have been observed in patients with cirrhosis. However this does not correlate with the presence or degree of Hepatic Encephalopathy.

Studies using Magnetic resonance spectroscopy (MRS) have shown a decrease in myo-inositol/creatine and choline/creatine ratios in white matter with an increase in the Glx (glutamine and glutamate) concentration in the basal ganglia in those with MHE. [64, 65] However, its usefulness in diagnosis of MHE has not been firmly proven.

MHE IN CHILDREN WITH EHPVO

While the prevalence and impact of MHE has been well studied in adults with EHPVO, the existence of MHE and its impact on the normal psychosocial development has not been explored in children. Since MHE obtunds attention span, alertness, reaction times, information processing and memory, its potential impact on the developing mind cannot be overemphasized. Whether MHE in EHPVO affects the child's overall intellectual and psychological development, as well as its possible impact on his/her scholastic performance remains to be studied.

The problem of analysing this is further complicated by the lack of any standardized tests that have been validated for diagnosing MHE in paediatric population. There is no normative data available for the use of the psychometric tests commonly used to detect MHE. It remains to be seen if the same tests that are applicable in adults would also be useful in children with MHE. The usefulness of CFF has also not been established in children with EHPVO.

Establishing the prevalence of MHE in children with EHPVO is therefore a challenge that needs to be addressed earnestly. Doing so would lay the foundation for treatment modalities for these children which may have the potential to improve their overall intellectual, psychological and social development.

AIMS OF THE STUDY

- To study the clinical profile of children with Extra-Hepatic Portal Vein Obstruction

- To study the prevalence of minimal hepatic encephalopathy in these children, using
    1. Psychometric Tests
    2. Critical Flicker Frequency

MATERIALS AND METHODS

STUDY DESIGN: Cross-sectional case-control observational study

STUDY CENTRE:

Madras Medical College & Rajiv Gandhi Government General Hospital and Institute of Child Health, Chennai

STUDY PERIOD: July 2013- Feb 2014

SAMPLE SIZE:

- 30 CASES
- 30 CONTROLS

INCLUSION CRITERIA:

- Children diagnosed to have EHPVO according to the definition by the Baveno V Consensus
- Age group – 8 to 18 years
- Doppler showing Portal Cavernoma

EXCLUSION CRITERIA:

Children with

- Acute/Chronic parenchymal Liver Disease
- jaundice or portal biliopathy
- shunt surgery in the past
- known neurological/psychiatric disease
- non-hepatic encephalopathies
- children on psycho-active drugs
- significant co-morbid illness

METHODOLOGY

Children diagnosed with EHPVO, on follow up at the Gastroenterology Department of Rajiv Gandhi Government General Hospital and Institute of Child health who satisfied the inclusion and exclusion criteria were taken up into the study.

PILOT STUDY:

An initial pilot study was done to determine the sample size and the same methodology was carried over to the actual study.

In each case, a detailed history was taken to ascertain the possible aetiology of EHPVO. History of umbilical sepsis, neonatal umbilical vein catheterisation, abdominal trauma, abdominal surgeries, and abdominal sepsis was elicited. The age at diagnosis, number of episodes of variceal bleeds, the number of years since the first bleed and the number of endotherapies performed were all recorded.

A thorough clinical examination including anthropometric data, general examination and per abdomen findings were noted. The anthropometric data was plotted against IAP Growth charts separate for Indian Girls and boys. The percentile under which their height for age falls was noted. If a child's weight was found to be less than the third percentile of the population for the particular age group, it was taken to signify growth retardation.

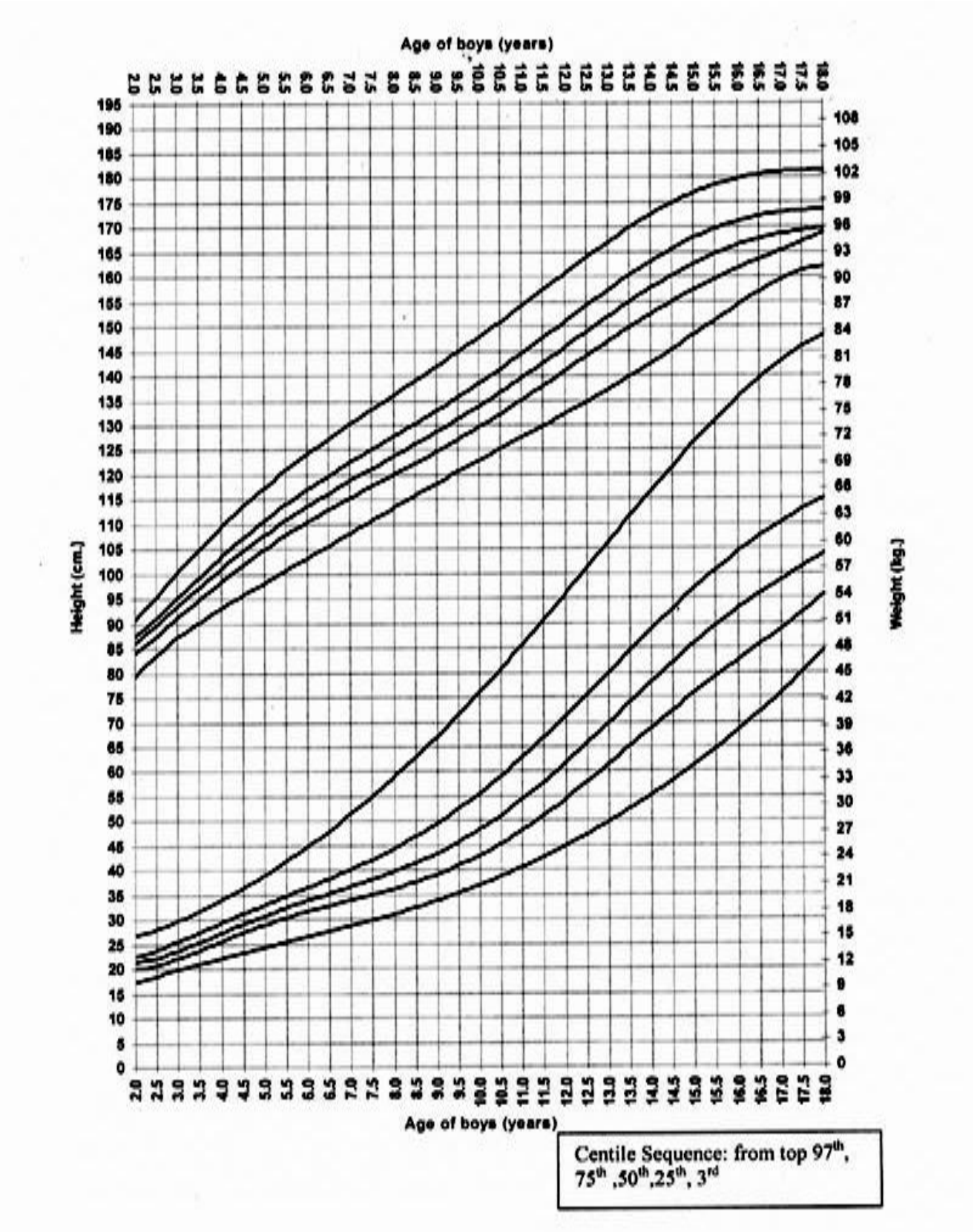


Figure 3: IAP Growth chart for Indian Boys -2-18 yrs

Complete hemogram, Liver function tests, serological markers of chronic viral hepatitis –HBsAg and Anti HCV were performed. Portal venous Doppler was done to confirm the diagnosis. Upper GI endoscopy findings, with respect to the presence and grade of oesophageal and gastro-oesophageal varices were collected from the child's medical records.

CONTROLS:

Controls were selected from a school in Chennai, so as to match the study group with respect to age and the class of study at school. The psychometric and CFF testing was done in the study group and the normative data was compiled.

PSYCHOMETRIC TESTS:

The following psychometric tests were performed in all the children.

1) Number Connection Tests A & B & T
2) Digit Symbol Test
3) Serial dot test
4) Line tracing test and

NUMBER CONNECTION TESTS A, B & T

These simple trail making, 'paper-pencil' tests were carried out and the time taken to complete each test was recorded. If the child were to make an error in these tests, it was quickly pointed out and corrected and the time recorded was the time included for correction. The Number connection Test –T was devised to nullify the disadvantage that children who had the medium of instruction as Tamil, had while performing NCT-B test. Each test was preceded by a sample test to ensure that the child understood what was required of her/him.

NUMBER CONNECTION TEST - A

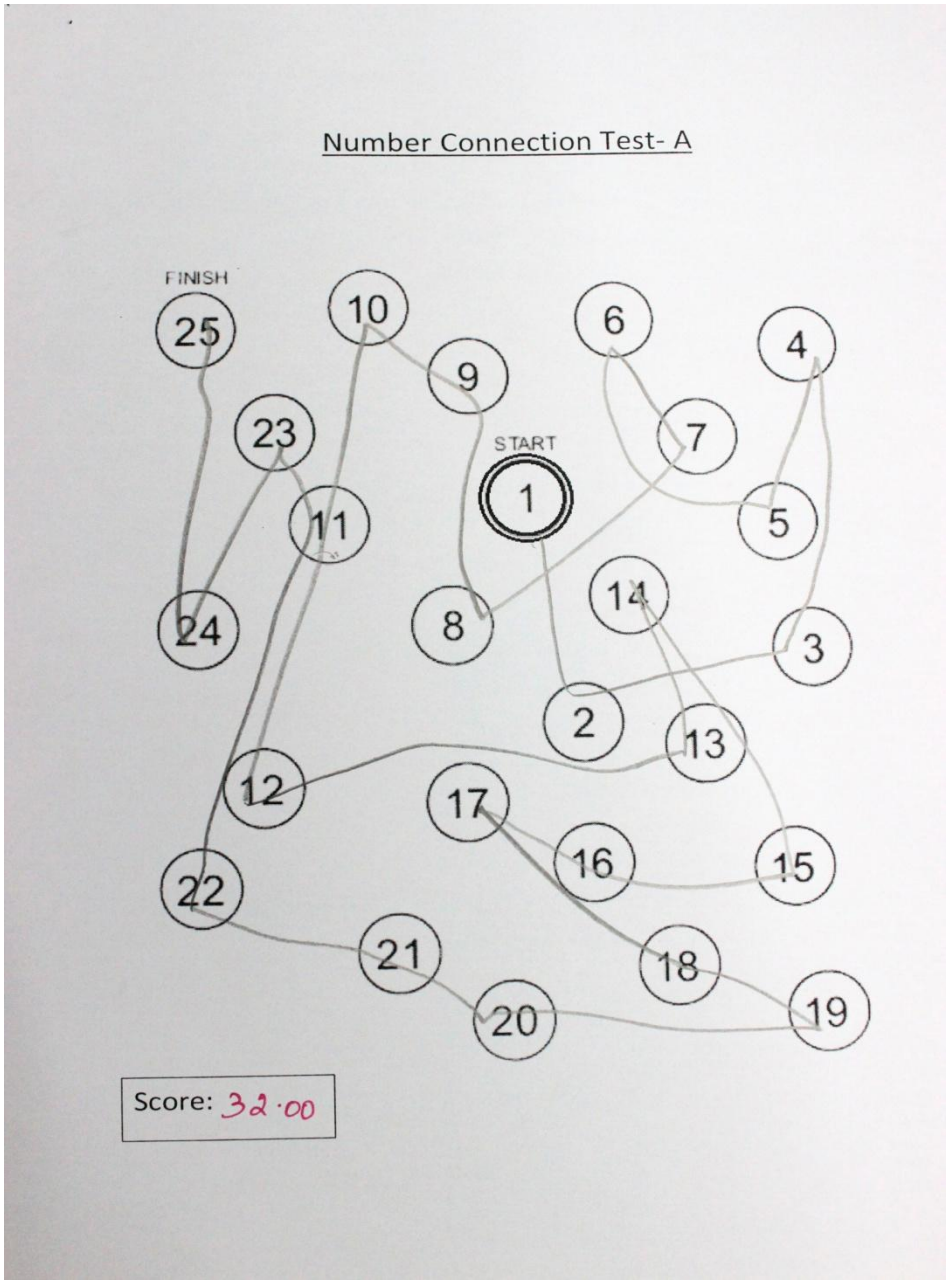


Figure 4: NCT- A

The child is asked to join one numeral to the next in ascending order and the time taken to complete the entire sequence is noted in seconds.

NUMBER CONNECTION TEST - B

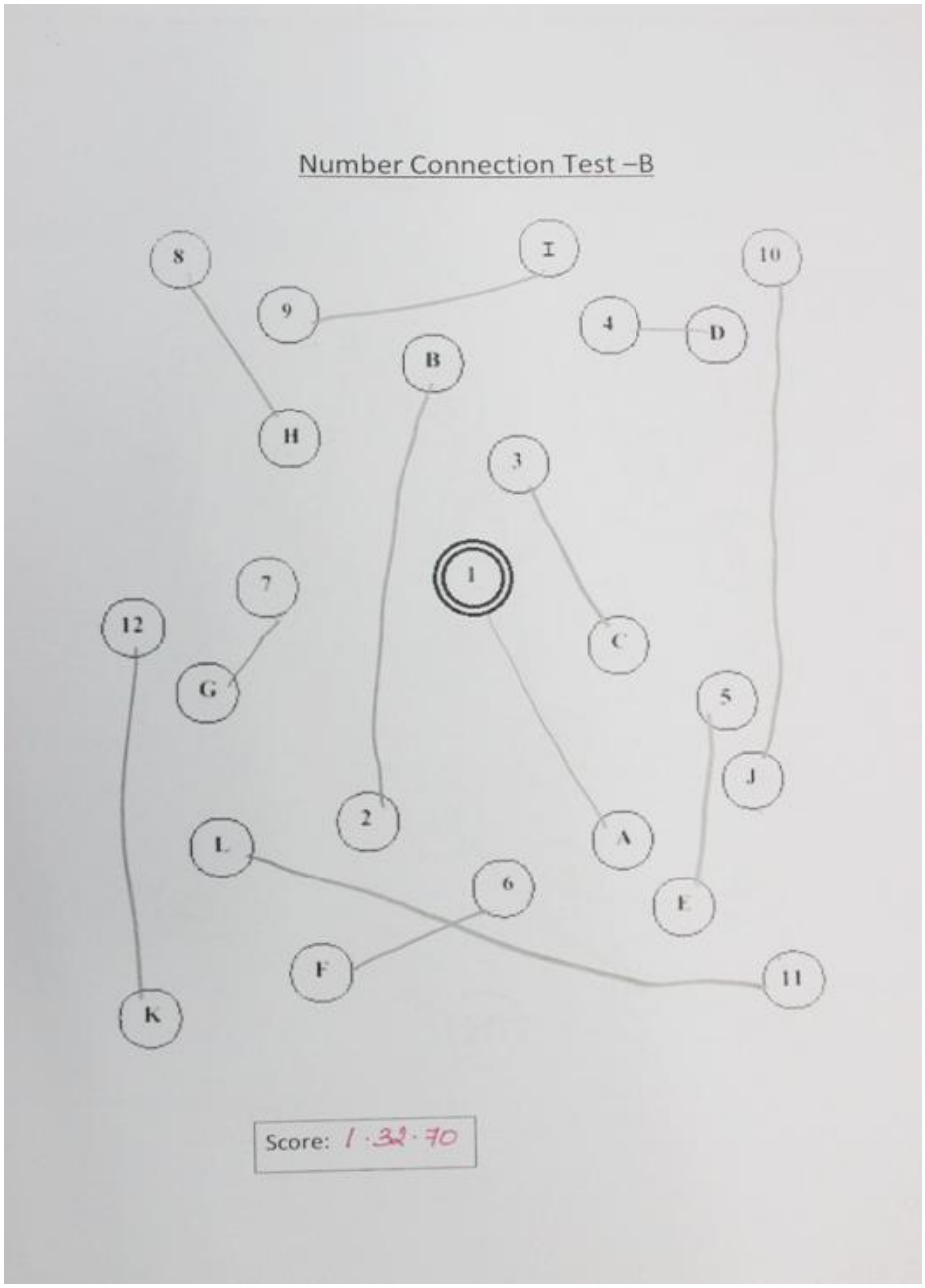


Figure 5: NCT - B

The child is asked to join the numerals to their corresponding alphabet and the time taken to complete the sequence is noted in seconds.

NUMBER CONNECTION TEST – T

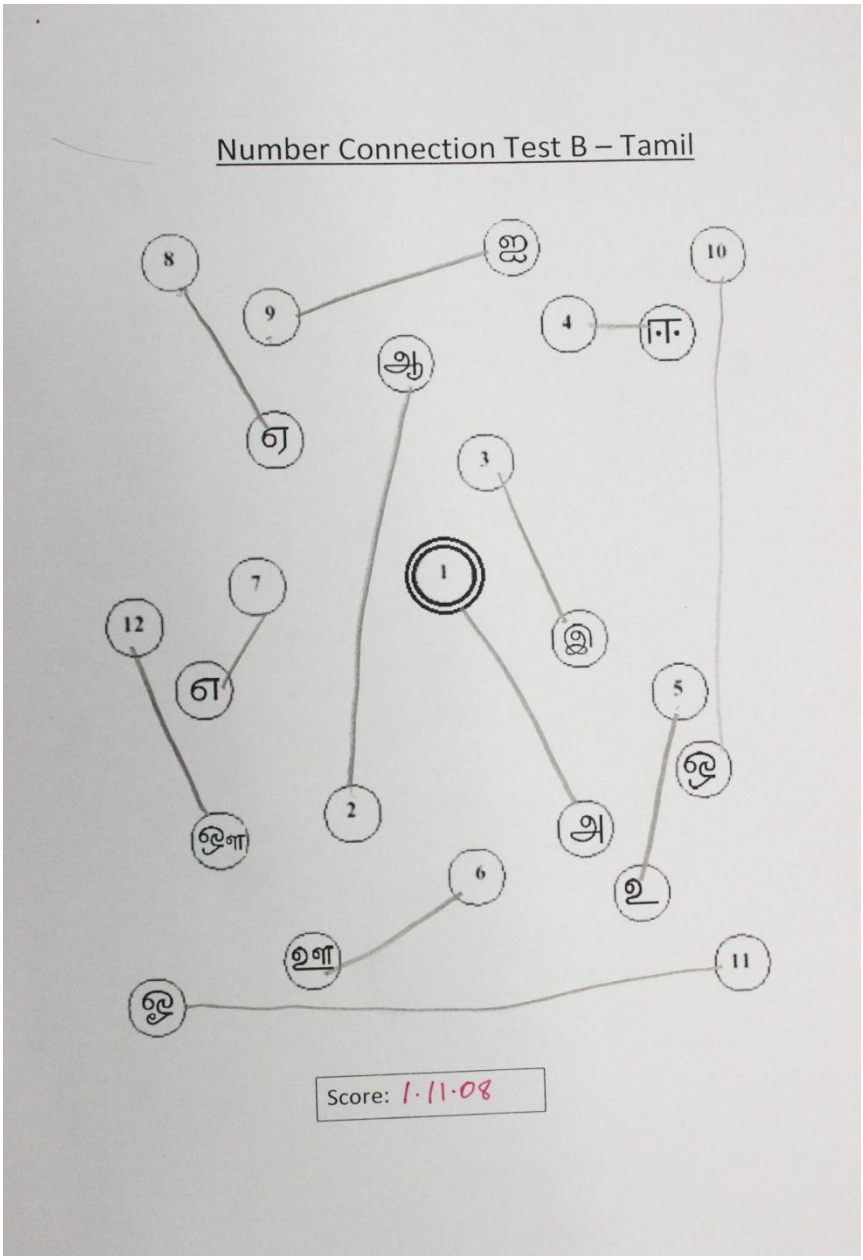


Figure 6: NCT - T

The child is asked to join each numeral with the corresponding Tamil alphabet in sequence. The time taken to complete the test is noted in seconds.

DIGIT SYMBOL TEST

This test requires the child to substitute a symbol below each numeral according to a key. The time required for the child to complete three rows of the test was noted. This too had a practice run before the actual test.

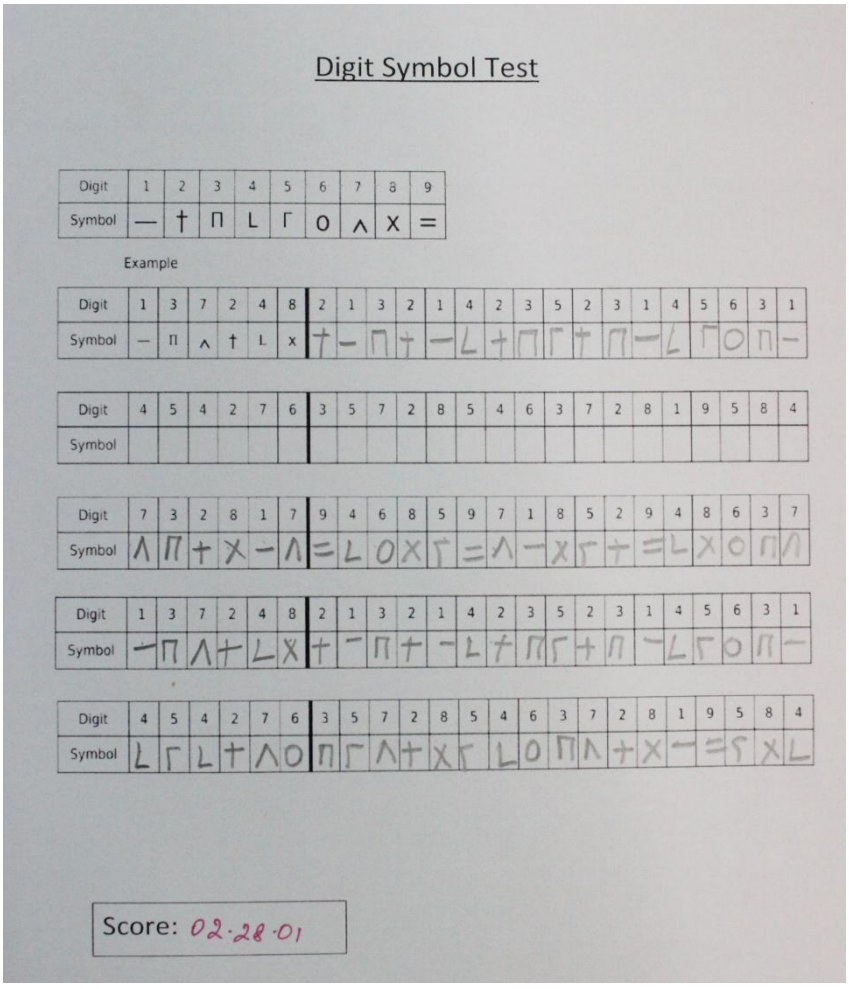


Figure 7: Digit Symbol Test

SERIAL DOTTING TEST

This test requires the child to keep dots serially approximately at the centre of the circles. The time required to complete the chart was the score of the test.

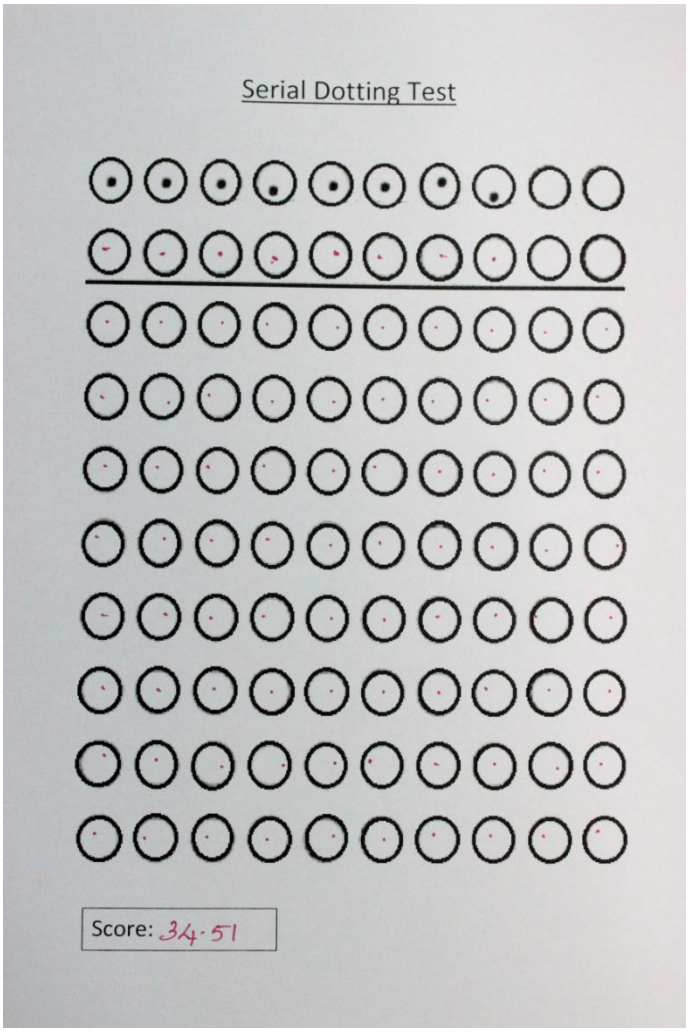


Figure 8: Serial Dotting Test

LINE TRACING TEST

The child was required to trace a line using a pencil, within the track in the picture without. The time required to complete the trail was the score. Penalty seconds were added for touching the track borders.

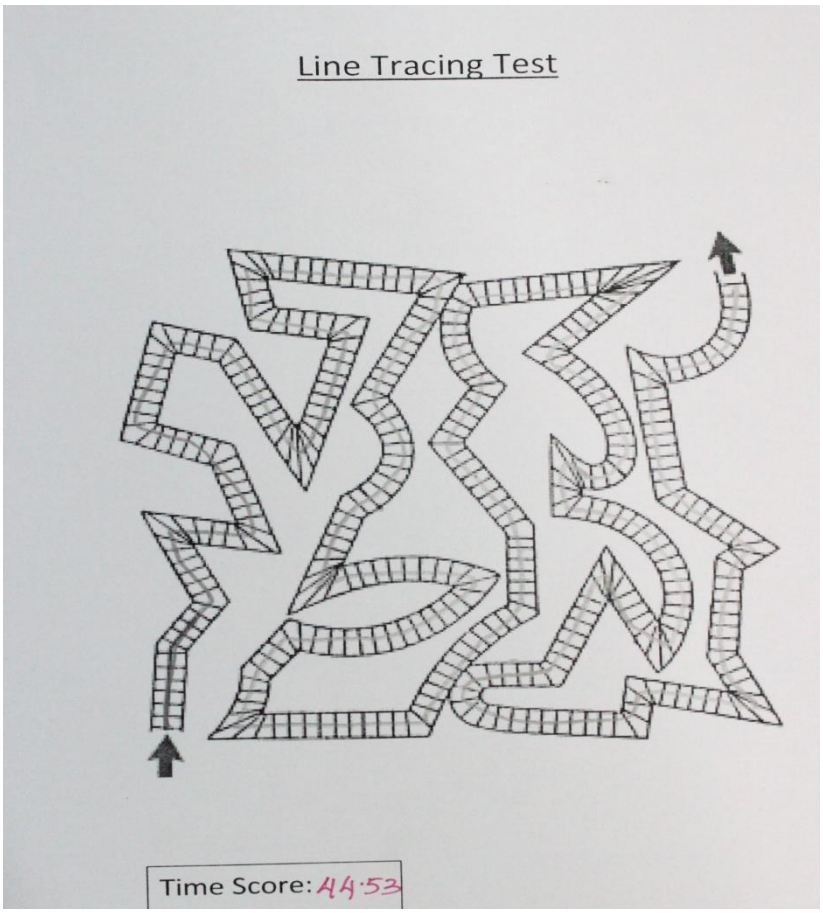


Figure 9: Line Tracing Test

CRITICAL FLICKER FREQUENCY ESTIMATION:

This was carried out using MEDIGRAPH CFF apparatus. The flicker frequency of the instrument ranged from 5 to 70flickers per second. The light source had the option of green and red light. Only red light was used in all the recordings. All recordings were made in a semi-darkened room by slowly increasing the frequencies until the flickering was perceived as a continuous light. This frequency was noted. Four consecutive readings were recorded and the mean was calculated as the critical flicker frequency.

Figure 10: MEDIGRAPH –CFF APPARATUS

STATISTICAL ANALYSIS

The sample size of 60 [30 cases and 30 controls] was calculated based on the pilot study values done for 7 cases and 7 controls. G Power 3.0.10 software was used. The α value was set at 0.05 and the sample size was calculated for a power of 0.95. Data processing was done using the software packages SPSS. Mean and standard deviation was calculated. Levene's Test for Equality of Variances and t-test for Equality of Means was used for comparison between cases and controls. Pearson Chi square test and Fischer's exact test was used for correlation between tests.

RESULTS

Table 1: BASELINE CHARACTERISICS OF THE CASES

CHARACTERISTICS	MEAN +/- SD [RANGE]
AGE	10.67± 1.32 yrs
SEX [M:F]	12:18
AVERAGE AGE AT DIAGNOSIS / RANGE	6.47 yrs /[1-12 YEARS]
AVERAGE YEARS SINCE DIAGNOSIS	4.2 yrs
BLEEDERS vs NON-BLEEDERS	29:1
NO. OF EPISODES OF BLEED [RANGE]	1.83 [0-10]
AVERAGE NUMBER OF ENDOTHERAPIES	10.93 [0-23]
HAEMOGLOBIN	10.51 [8.9-12] gm%
BILIRUBIN	0.86 [0.6-1.2] mg/dl
AST	27.83[22-34] IU/L
ALT	27.57[18-36] IU/L
ALBUMIN	3.63[3.4-3.9] gm/dl

Table 2: BASELINE CHARACTERISTICS OF CONTROLS

AGE	10.67± 1.32
SEX [M:F]	10:20

AGE:

The average age of the cases was 10.67 years. The range was from 8 to 13 years. The average age of the controls was identical to the control group, since they were matched before enrolling them for the tests

SEX DISTRIBUTION:

There were totally 12boys [40%] and 18 girls [60%] in the study.

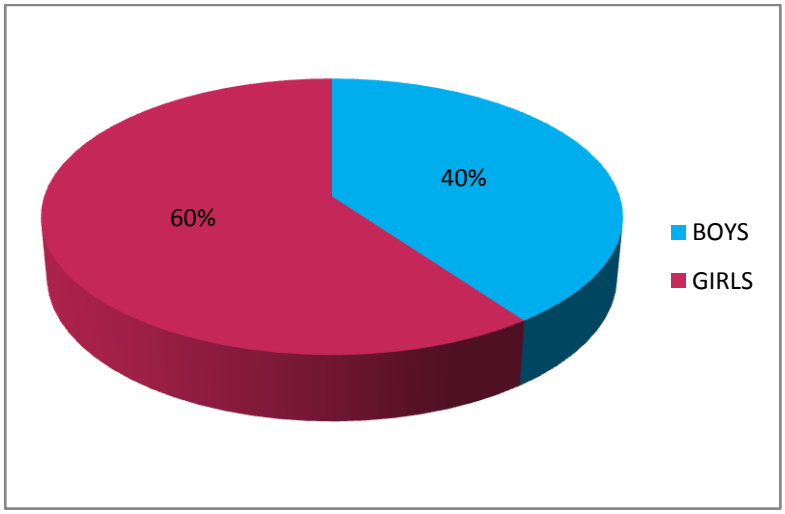


Chart 1: Sex distribution of Cases

MODE OF INITIAL PRESENTATION

The most common mode of initial presentation was variceal bleed in 80%, followed by abdominal mass in 14%. Fever and anaemia were presenting features in 3% each.

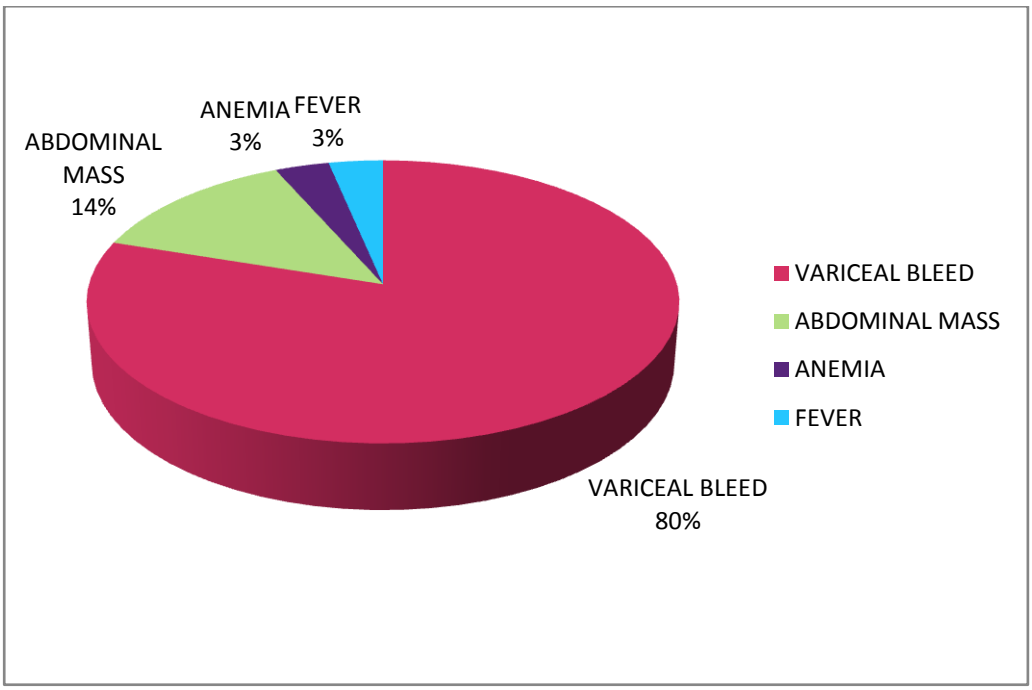


Chart 2: Mode of Initial Presentation

AETIOLOGY

In most of the children, no antecedent etiological history could be elicited. A history suggestive of umbilical sepsis was present in 6 children.

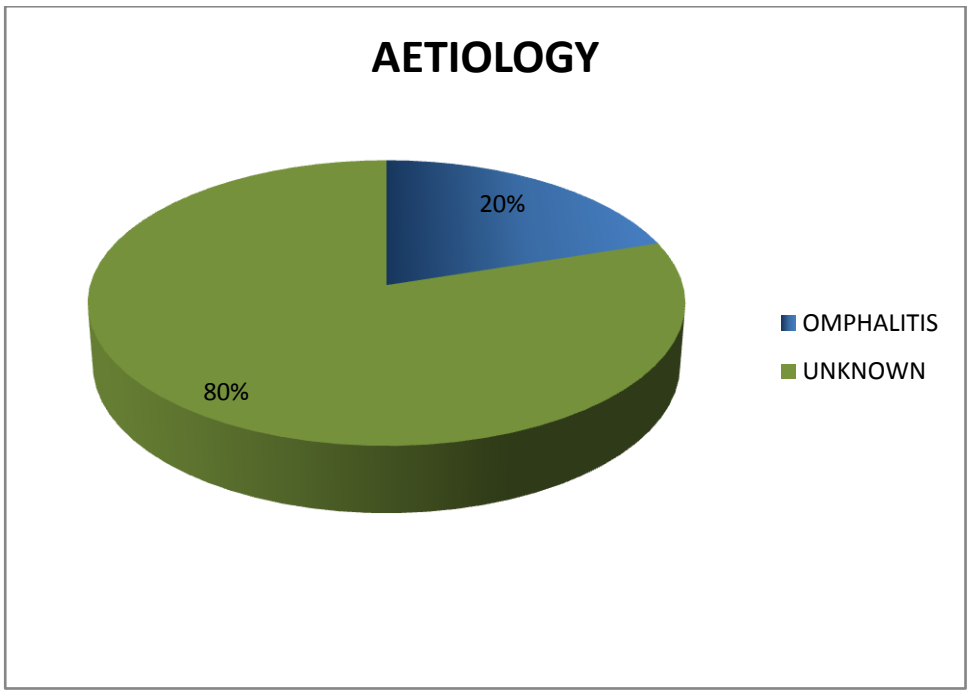


Chart 3: Aetiology of EHPVO

VARICEAL BLEEDING

Out of the thirty children, only one child was not a bleeder [3% vs 97%]. But he too had evidence of varies at endoscopy. The number of episodes of bleeding was quite variable with a range of 1 to 10 with a mean of nearly 2 episodes. Most of the patients [87%] had had a history of endotherapy. The average number of endotherapies performed one each child was 11 and it ranged from 0 to 23.

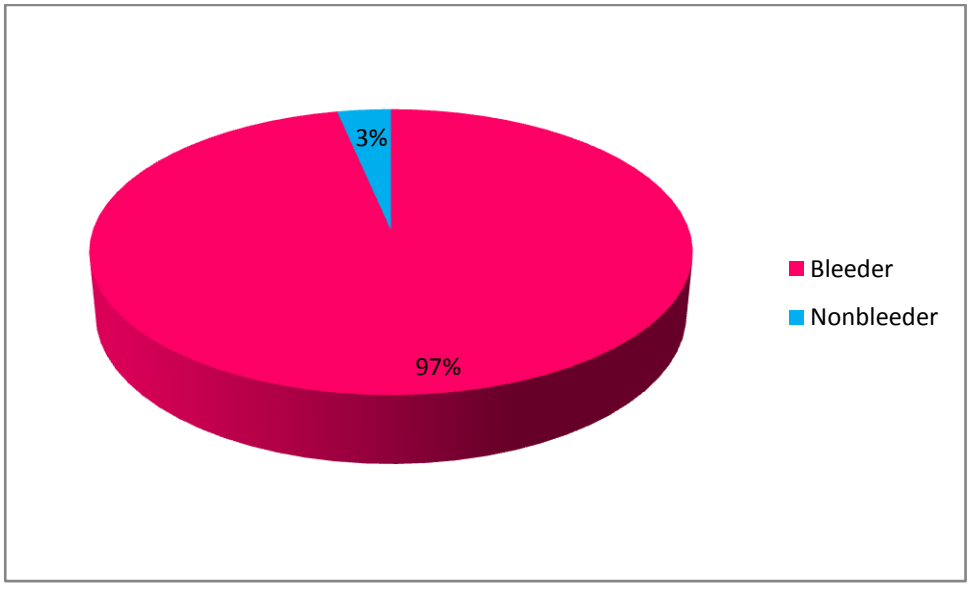


Chart 4: Bleeders vs Non-bleeders

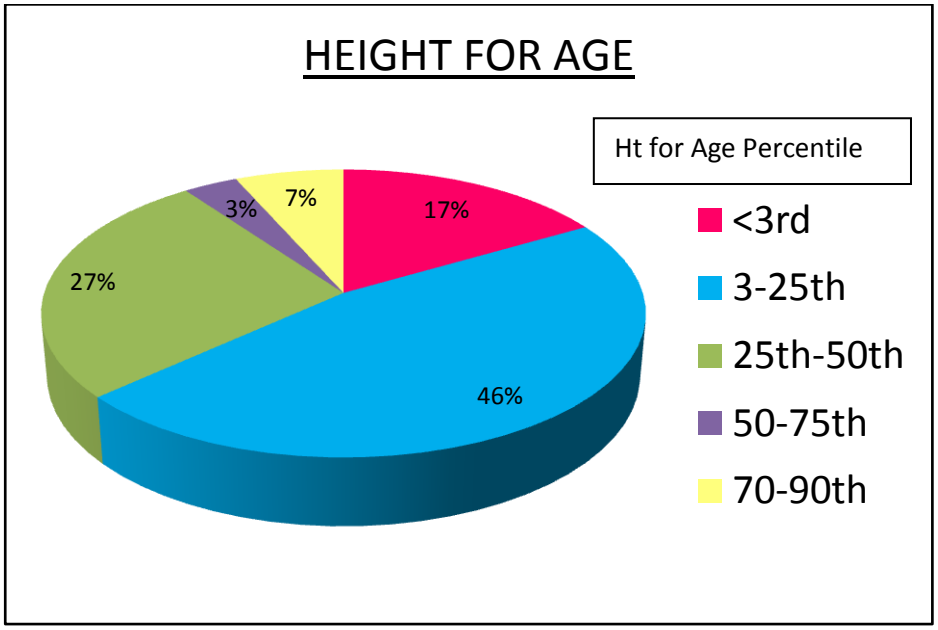
GROWTH RETARDATION:

The distribution of the study population according to the growth percentile is as given below.

Table 3: Height for age

HT FOR AGE	CASES	PERCENTAGE
<3rd percentile	5	**17%**
3-25th	14	46%
25th-50th	8	27%
50-75th	1	3%
70-90th	2	7%

Chart 5: Height for age, distribution



Most of the children were between the 3rd and 25th percentile for ht appropriateness for age. 5 children [17%] had an ht less than the 3rd percentile for age signifying growth retardation.

UPPER GI ENDOSCOPY:

All thirty cases had varices at upper GI endoscopy.

Table 4: Type of Varix

VARIX	NUMBER Of CHILDREN
SMALL ESOPHAGEAL VARIX	6
LARGE ESOPHAGEAL VARICES	16
GOV	18

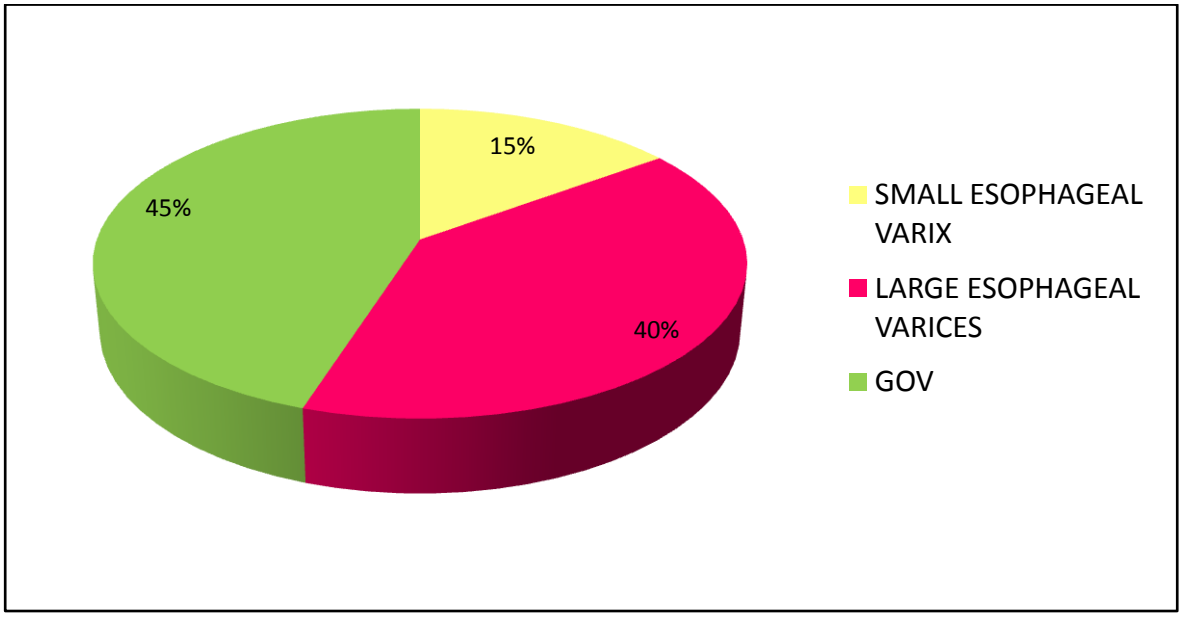


Chart 6: Type of Varix at Endoscopy

PSYCHOMETRIC TEST SCORES

The mean normative scores derived from the control group for NCTA was 46.17±19.44, for NCT-B -77.53±26.66, NCT-T70.83±30.38, DST - 140.4±20.09, SDT - 46.77±9.88 and LTT - 54.97±11.66. The mean score for the study group was NCT-A- 73.9±32.87, NCT-B-148.87±71.7, NCT-T-108.37±43.62, DST - 236.00±89.63, SDT - 53.53±14.06 and LTT - 72.53 ± 19.06

Table 5: Psychometric Test Scores – Comparison of Means

TEST	CONTROLS [Sec]	CASES [Sec]	SIGNIFICANCE [p value]
NCT-A	46.17±19.44	73.9±32.87	<0.001
NCT-B	75.3±26.66	148.87±71.7	<0.001
NCT-T	70.83±30.38	108.37±43.62	<0.001
DST	140.4±20.09	236.00±89.63	<0.001
SDT	46.77±9.88	53.53±14.06	0.036
LTT	54.97±11.66	72.53±19.06	<0.001

The mean scores for the cases were higher than those of the controls. The difference between the mean test scores between the control group and study group was statistically significant for all the tests.

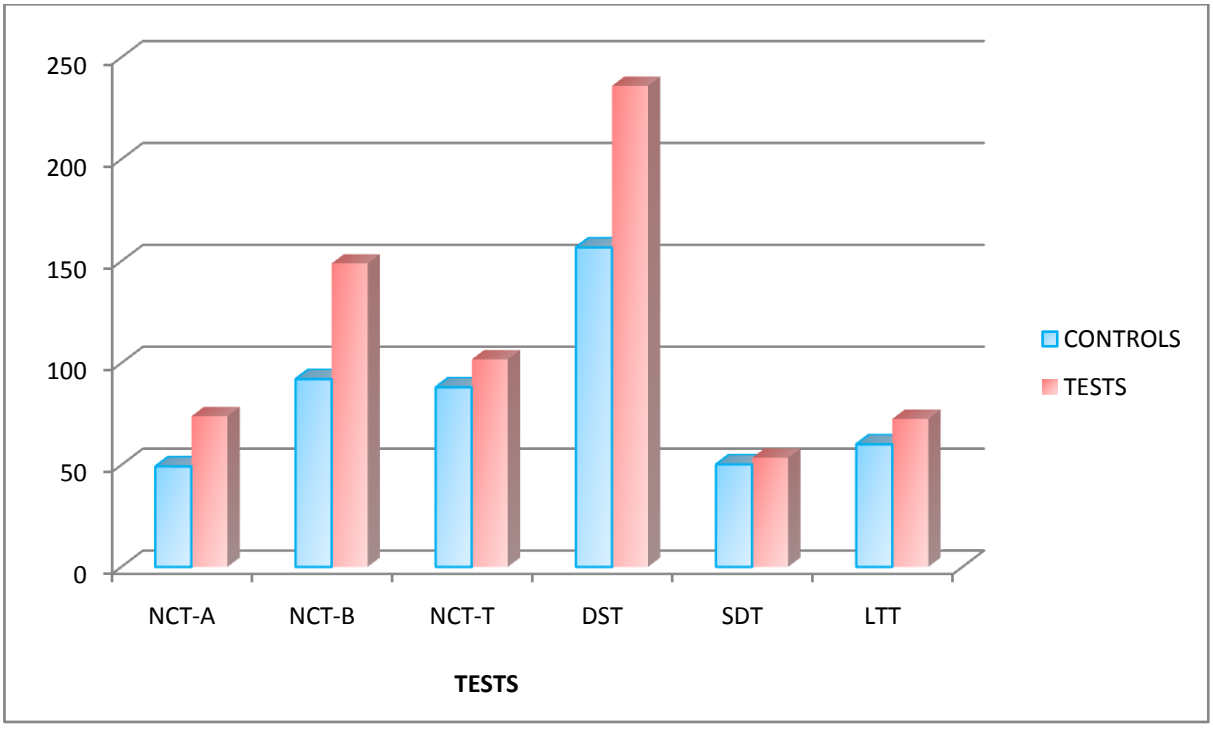


Chart 7: Psychometric Test Scores – Comparison of Means

PSYCHOMETRIC TEST RESULTS

The prevalence of abnormal psychometric tests in the study group according to each test is as follows… NCT-A - 9[30%], NCT-B - 15 [50%], NCT-T - 9[30%], DST - 18[60%] , SDT - 3[10%] , LTT - 9[30%] . Minimal hepatic encephalopathy was said to be present if at least two psychometric tests were abnormal [>2S.D from mean]. Accordingly, MHE was present in 15 of the children. Except for serial dotting test, all tests correlated individually with the presence of MHE.

Table 6: Yield of each individual test

TEST	Abnormality in cases	Corrrelation with MHE [p value]
NCT-A	9[30%]	0.001
NCT-B	15 [50%]	0.001
NCT-T	9[30%]	0.001
DST	18[60%]	0.001
SDT	3[10%]	**0.068**
LTT	9[30%]	0.005

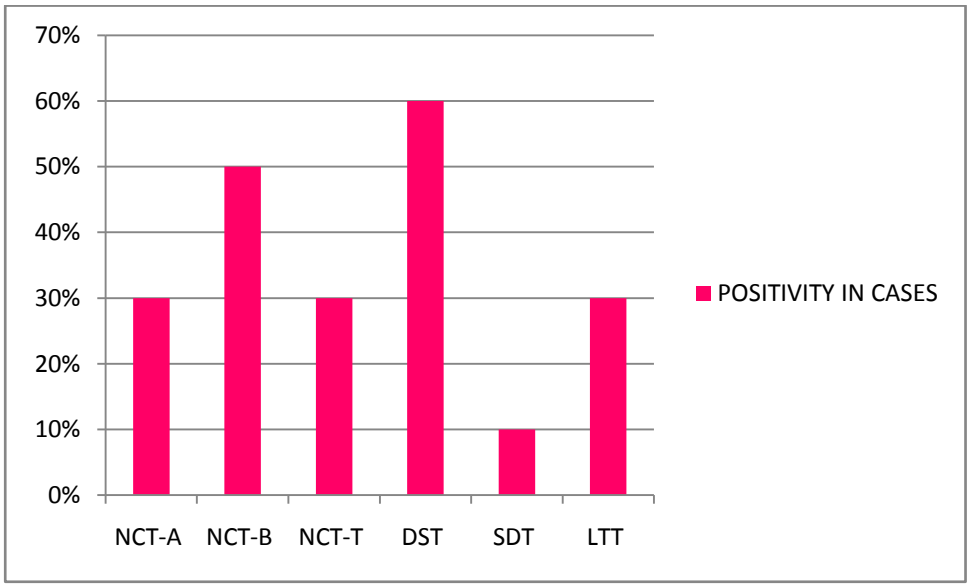


Chart 8: Yield of each Psychometric Test

The sensitivity and specificity of each test for predicting MHE is as follows.

Table 7: Sensitivity and Specificity of each psychometric test for MHE

TEST	SENSITIVITY	SPECIFICITY
NCT-A	60 %	100 %
NCT-B	86.67 %	86.67 %
NCT-T	60 %	100 %
DST	100 %	80 %
SDT	20 %	100 %
LTT	53 %	93 %

CRITICAL FLICKER FREQUENCY

The mean CFF value of the control group was 48.05 with a S.D of 1.12 flickers. The cut off for detecting MHE was 45.8 [< 2 S.D of mean]. The mean CFF of the cases was 46.016.

Table 8: CFF controls vs Cases

	CONTROLS	CASES	p value
CFF	48.05±1.12	46.016	<0.001

The sensitivity and specificity of CFF in predicting MHE with respect to PHES was 80% and 86% respectively.

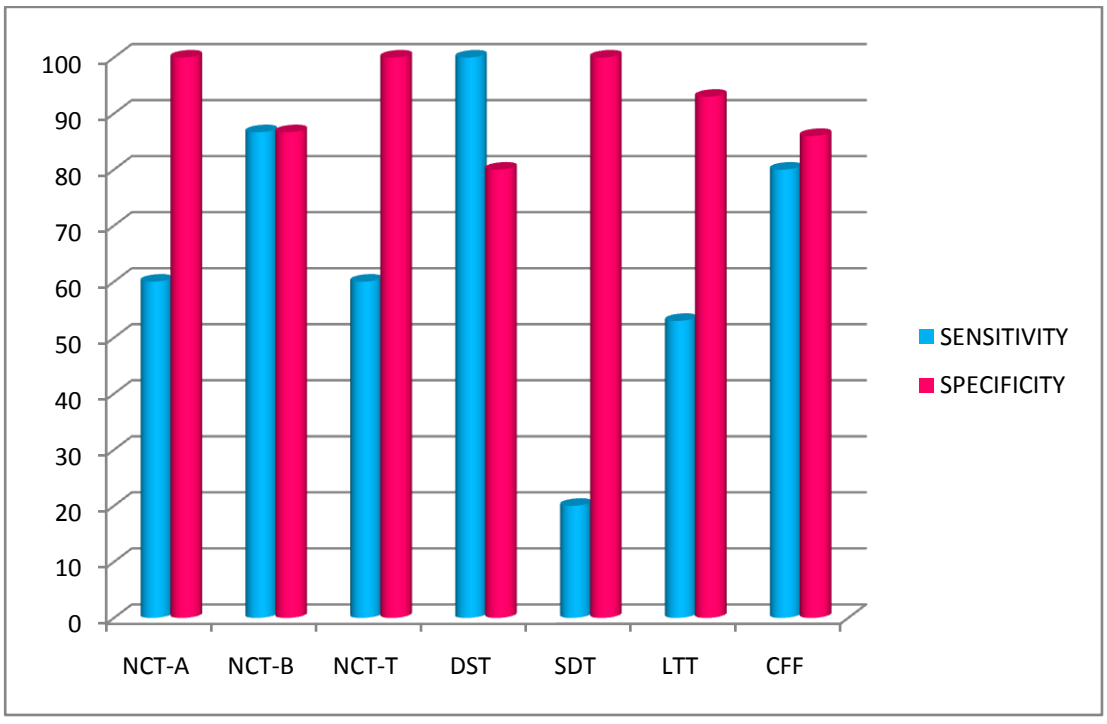


Chart 9: Sensitivity and Specificity of each psychometric test and CFF

DISCUSSSION

In this study the clinical profile of children with EHPVO and the prevalence of Minimal Hepatic Encephalopathy were studied using psychometric tests and critical flicker frequency.

All the children in our study were chronic forms of EHPVO, on follow up at the gastroenterology OPD. All of them had evidence of portal cavernoma on portal doppler imaging.

The most common mode of initial presentation of the cases was with an episode of variceal bleeding. Eighty percent of children had presented with an episode of variceal bleed. Studies by Arora et al [27] and Poddar [25] have shown that variceal bleeding is the presenting feature in 85%-90% of cases, similar to our study. In our study abdominal mass was the presenting feature in 14% of cases. One child had been admitted for fever and during evaluation, was found to have underlying chronic EHPVO and another was found to have EHPVO while being evaluated for anaemia and splenomegaly.

History suggestive of neonatal umbilical sepsis was forthcoming in 6 cases. Most of these children had been delivered at home. In nearly 80% of the cases, no antecedent cause could be elicited in their history. Studies by Poddar et al have shown that nearly 90% of cases of EHPVO are idiopathic.[24] The reason probably lies in the fact that most acute forms of

EHPVO have minimal clinical features and thus are often overlooked. As the disease becomes chronic, it presents more dramatically, by which time the initial acute event is not correlated with.

The anthropometric data of our study suggests that nearly 17% of them were short statured; that is their height for age was less than the 3rd percentile for Indian children. According to the study by Mehrotra R N, Batia V et al, the prevalence of growth retardation in children with EHPVO was as high as 50%.[36] But the definition of growth retardation taken in this study was a height less than the 5th percentile, instead of the 3rd percentile. Therefore, the prevalence of growth retardation was overestimated in this study.

Twenty nine out of the thirty children with EHPVO had a history of variceal bleed. At endoscopy 85% of them had large varices. Though literature states that nearly 70% have gastric varices, [26, 27] in our study only 45% of the children had gastric varices- all in conjuction with oesophageal varices. None of them had isolated gastric varices.

All the children were able to complete the psychometric tests in our study. The number connection tests B and T were the most difficult and most prone for corrections. The NCT-T was introduced in our study to eliminate the disadvantage a child might have due to differences in their language of instruction at school. There were differences in the mean

scores between NCT-B and NCT-T in both groups. The NCT-T test had a lower mean score compared to NCT-B in both the groups; though essentially these tests are identical except for the language used. This suggests that regional language has a great role to play when it came to arriving at normative data for psychometric tests in a particular population. Ours being a diverse population with respect to language, normative data of NCT-B in different regional languages tests would probably be required in studies in the Indian population. Figure connection tests can overcome this problem, but are more time consuming than the NCT tests.

In our study the mean score of all the tests were higher in the study group compared to the controls. This difference was statistically significant for all the tests [p value <0.05]. When compared between the cases and control groups the difference in the average score were higher for the DST and the NCT-B tests. These tests also had the highest sensitivity in detecting Minimal Hepatic Encephalopathy. They were also the least specific. It may well serve that these two tests can be used as screening tests and if positive, the child can be subjected to the entire battery of tests.

The prevalence of MHE in our study was 50% according to psychometric analysis; i.e. 15 children had two or more test scores which were abnormal. The test score was said to be abnormal if it was greater

than 2 S.D from the control group. Studies on in adults with EHPVO have shown that the prevalence of MHE in them to be around 40-45%.[67-68] The inclusion of an additional test in the form of NCT-T probably explains the slightly higher incidence in our study. The proposed pathogenic mechanism behind the pathogenesis of MHE in EHPVO is the chronic porto-systemic shunting of blood bypassing the liver. In our study we found no statistically significant association between the duration of the disease and the presence of minimal hepatic encephalopathy.

Critical Flicker frequency estimation was done in the control and study population. The test was carried out after explaining the test in detail and it was made sure before the test that they understood what was expected of them in this test. . The instrument used was the Digital Critical Flicker fusion apparatus from MEDI-Systems India. Consequently the same cut-off of 38 Hz used in other studies which have used the HEPATOnorm CFF analyzer- Germany, could not be adopted in our study. The cut-off in our study was derived from the CFF thresholds obtained using our instrument in the control group. Fourteen children with EHPVO had an abnormal CFF reading compared to the controls. CFF had a good consistency in predicting MHE detected based upon psychometric tests. The sensitivity and specificity of CFF in detecting MHE was 80% and 86% respectively in our study. In the study by Manuel Romero –Gomez et al,

similar rates of sensitivity [76.2%] but a slightly lower rate of specificity [61.4%] was reported for CFF in detecting MHE.[63] But in this study it was entirely an adult population which was assessed.

The impact of MHE on the child's overall intellectual development needs to be analysed further. Whether the presence of MHE has a bearing on the child's academic performance is also an area of research that has to be explored. If it were the case, then it would deem fit that these children received additional care, assistance and support with their curricular work and endeavours. Treatment modalities have been tried and have been shown to be beneficial in MHE occurring in adult patients with EHPVO. [68] The scope for similar treatment modalities in EHPVO children with MHE merits future studies.

CONCLUSIONS

1. Minimal Hepatic Encephalopathy does exist in children with Extra Hepatic Portal Vein Obstruction.
2. Prevalence is as high as 50% when psychometric tests are used and 46% when Critical Flicker Fusion is used.
3. Digit Symbol Test, Number Connection Test - B are highly sensitive among psychometric tests in detecting Minimal Hepatic Encephalopathy and can be used as initial screening tests.
4. Critical Flicker Fusion has a good sensitivity and specificity in detecting Minimal Hepatic Encephalopathy and correlated well with psychometric tests.

BIBLIOGRAPHY

1. Sarin S.K., Sollando J.D., et al. Consensus on extra-hepatic portal vein obstruction. *Liver int 2006; 26:512-9*
2. Yachha S K, Khandur A, Sharma B C, Kumar M. Gastrointestinal bleeding in children. *J Gastroenterol Hepatol 1996; 11: 903–7*
3. Valla D C , Condat B, Lebrec D. Spectrum of portal vein thrombosis in the West. *J Gastroenterol Hepatol 2002; 17(Suppl. 3): S224–*7
4. Stringer MD, Heaton ND, Karani J., et al. Patterns of portal vein occlusion and their etiological significance. *Br J Surg 1994; 81: 1328–31.*
5. Ya dav S , Dutta A K, Sarin S K. Do umbilical vein catheterization and sepsis lead to portal vein thrombosis?- A prospective, clinical and sonographic evaluation*. J Pediatr Gastroenterol Nutr 1993; 17: 392–6.*
6. Odievre M, Pige G, Alagille D. Congenital abnormalities associated with extraheptic portal hypertension. *Arch Dis Child 1977; 52: 383–5.*
7. Bhattacharya M, Makhani G, Kannan M, Ahmed R P, Gupta P K, Saxena R. Inherited prothrombotic defects in Budd–Chiari syndrome and portal vein thrombosis: a study from North India. *Am J Clin Pathol 2004; 121: 844–7.*

8. Webb L J, Sherlock S. The aetiology, presentation and natural history of extra-hepatic portal venous obstruction. *Q J Med 1979; 192: 627–39.*
9. Romero-Gomez, Boza F et al. Subclinical hepatic encephalopathy predicts the development of overt hepatic encephalopathy. *Am J Gastroenteology 2001;96:2718-23*
10. Das A, Dhiman RK et al. Prevalence and natural history of subclinical hepatic encephalopathy in cirrhosis. *J gastroenerol Hepatol 2001; 16: 531-5*
11. Hartmann lj, Groeneweg et al. The prognostic significance of subclinical hepatic encephalopathy. *AM J Gastroenerol 2000; 95:2029-34*
12. Sharma P, Sharma BC, Puri V et al. Minimal Hepatic encephalopathy in patients with EHPVO. *Am J of Gastroenterol 2008;103:1406-1412*
13. Sharma P, Sharma BC, Puri V et al. Natural History of minimal hepatic encephalopathy in patients with EHPVO. *Am J of Gatroenterology 2009; 104:885-90*
14. Goel A, Yadav S. Cerebral oedema in MHE due to EHPVO. *Liver Int 2010;30:1143-51*
15. Roberto de Franchi at al Revising consensus in portal hypertension: Report of the Baveno consensus workshop on methodology of

diagnosis and therapy in portal hypertension - *Journal of Hepatology 2010 vol. 53 762–768*

16. Sarin S.K, Sollando et al. Consensus on extra-hepatic portal vein Obstruction - *Liver International 2006: 26: 512–519*
17. Valla D C , Condat B, Lebrec D. Spectrum of portal vein thrombosis in the West*. J Gastroenterol Hepatol 2002;17(Suppl. 3): S224–7.*
18. Poddar U, Thapa BR, Rao KL, Singh K. Etiological spectrum of esphageal varices due to portal hypertension in Indian children: is it different from the West? *J Gastroenterol Hepatol. 2008;23:1354–7.*
19. Yadav S , Dutta A K, Sarin S K. Do umbilical veincatheterization and sepsis lead to portal vein thrombosis?A prospective, clinical and sonographic evaluation. *J Pediatr Gastroenterol Nutr 1993; 17: 392–6.*
20. Odievre M, Pige G, Alagille D. Congenital abnormalities associated with extraheptic portal hypertension. *Arch Dis Child 1977; 52: 383–5.*
21. Bhattacharya M, Makhani G, Kannan M, Ahmed R P, Gupta P K, Saxena R. Inherited prothrombotic defects in Budd–Chiari syndrome and portal veiN thrombosis: a study from North India. *Am J Clin Pathol 2004; 121: 844–7*.
22. Pinto RB, Silveira TR, Bandenilli E, Rohsig L. Portalvein thrombosis in children and adolescents: the low prevalence of hereditary thrombophilic disorders. *J Pediatr Surg 2004; 39: 1356–61*.

23. Valla D , Casadevall N, Huisse M G, et al. Myeloproliferative disorders in portal vein thrombosis in adults. *GastroenteroL 1998; 94: 1063–9.*
24. Poddar U, Thapa BR, Singh K. Endoscopic sclerotherapy in children: experience with 257 cases of extra hepatic portal venous obstruction. *Gastrointest Endosc. 2003;57:683–6.*
25. Poddar U, Thapa BR, Rao KL, Singh K. Etiological spectrum of esphageal varices due to portal hypertension in Indian children: is it different from the West? *J Gastroenterol Hepatol. 2008;23:1354–7.*
26. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK. Prevalence, classification and natural history of gastric varices: a long-term follow up study in 568 portal hypertension patients. *Hepatology. 1992;16:1343–9*
27. Arora NK, Lodha R, Gulati S, Gupta AK, Mathur P, Joshi MS, et al. Portal hypertension in north Indian children*. Indian J Pediatr. 1998;65:585–91*.
28. Poddar U, Thapa BR, Singh K. Frequency of gastropathy and gastric varices in children with extra hepatic portal venous obstruction treated with sclerotherapy. *JGastroenterol Hepatol. 2004;19:1253–6.*
29. Heaton ND, Davenport M, Howard ER. Incidence of haemorrhoids and anorectal varices in children with portal hypertension. *Br J Surg.1993; 80:616–8*

30. Rector WG, Reynolds TB. Risk factors for haemorrhage from oesophageal varices and acute gastric erosions. *Clin Gastroenterol. 1985;14:139-153*

31. Arora NK, Ganguly S, Mathur P, Ahuja A, Patwari A. Upper Gastrointestinal bleeding: Aetiology and Management. *Indian J Pediatrics. 2002; 69:155-168.*

32. Mittal SK, Kalra KK, Aggarwal V. Diagnostic upper GI endoscopy for hematemesis in children: experience from a paediatric gastroenterology centre in north India. *Indian J Pedia.1994;61:651–4.*

33. Yachha S K, Khandur A, Sharma B C, Kumar M. Gastrointestinal bleeding in children. *J Gastroenterol Hepatol 1996; 11: 903-7*

34. Rangari M, Gupta R, Jain M, Malhotra V, Sarin S K. Hepatic dysfunction in patients with extra hepatic portal venous obstruction. *Liver Int 2003 Dec; 23: 434-9*

35. Poddar U, Borkar V. Management of extra hepatic portal venous obstruction (EHPVO): current strategies. *Tropical Gastroenterology 2011;32(2):94–102.*

36. Mehrotra RN, Batia V, Dabadghao P, Yachha SK. Extrahepatic portal vein obstruction in children: anthropometry, growth hormone, and insulin-like growth factor I. *J Pediatr Gastroent Nutr 1997;25:520-3*

37. Arora NK. (Principal Investigator), Mathur P, Das MK.. Project titled "Risk factors for rebleeding after endoscopic sclerotherapy in children with Extra hepatic Portal Hypertension" *Funded by Indian Council of Medical Research (ICMR).India, Report 2000*
38. Nihal N, Bapat MR, Rathi P, Shah NS, Karvat A, Abraham P, et al. Relation of insulin-like growth factor-1 and insulin-like growth factor binding protein-3 levels to growth retardation in extra hepatic portal vein obstruction. *Hepatol Int.* 2009;3:305–9.
39. Lautz TB, Sundaram SS, Whitington PF, Keys L, Superina RA. Growth impairment in children with extra hepatic portal vein obstruction is improved by mesenterico-left portal vein bypass. *J Pediatr Surg*. 2009;44:2067–70.
40. Stringer MD. Improved body mass index after mesenterico-portal bypass. *Pediatr Surg Int*. 2007;23:539–43.
41. Webb L J, Sherlock S. The aetiology, presentation and natural history of extra-hepatic portal venous obstruction. J Med 1979; 192: 627–39.
42. MinguezB, Garcia-Pagan JC et al Non- cirrhotic portal vein thrombosis exhibits neuro pscho-local and MR changes consistent with minimal hepatic encephalopathy

43. Ferenci P, Lockwood et al ,Hepatic encephalopathy – definition, nomenclature, diagnosis, quantification-final report of the World Cong. of Gastroenterology, Vienna,1998. *Hepatolo 2002 ;35:716 –2 1.*
44. Sarin SK , Nundy S .Subclinical encephalopathy after portosystemic shin patients with non-cirrhotic portal fibrosis. Liver 1985;5:142–6 .
45. Ferenci P,Lockwood A,mullen K, Tarter r, Weissenborn K at al Hepatic encephalopathy--definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th World Congresses of Gastroenterology, vienna, 1998. *Hepatology. 2002 mar;35(3):716-21*
46. Groeneweg M, Quero JC, de Bruijn I, Hartmann IJC, Essink-Bot ML, Hop WCJ, et al. Subclinical hepatic encephalopathy impairs daily functioning. *Hepatology 1998;28:45–49.*
47. Schiff S, Vallesi A, Mapelli D, et al. Impairment of response inhibition precedes motor alteration in the early stage of liver cirrhosis: A behavioral and electrophysiological study. *Metab Brain Dis 2005;20:381–92.*
48. Weissenborn K, Heidenreich S, Ennen J, et al. Attention deficits in minimal hepatic encephalopathy. *Metab Brain Dis 2001;16:13–9.*
49. Watanabe A, Tuchida T, Yata Y, Kuwabara Y. Evaluation of neuropsychological function in patients with liver cirrhosis with

special reference to their driving ability. *Metab Brain Dis* 1995;10:239–48.

50. Srivastava A, Mehta R, Rothke SP, Rademaker AW, Blei AT. Fitness to drive in patients with cirrhosis and portal-systemic shunting: a pilot study evaluating driving performance. *J Hepatol* 1994;21:1023–8.
51. Wein C, Koch H, Popp B, Oehler G, Schauder P. Minimal hepatic encephalopathy impairs fi tness to drive. *Hepatol* 2004;39:739–45.
52. Jasmohan S. Bajaj, M.D., Kia Saeian, M.D.et al Minimal Hepatic Encephalopathy: A Vehicle for Accidents and Traffic Violations - *Am J Gastroenterol 2007;102:1903–1909*
53. Prasad S, Dhiman RK, Duseja A, Chawla Y, Sharma A, Agarwa R. Lactulose improves Cognitive functions and health-relate quality of life in cirrhotic patients with minimal hepatic encephalopathy *Hepatology 2007;45: 549–59*
54. Schomerus H, Hamster W. Quality of life in cirrhotics with minimal hepatic encephalopathy. *Metab Brain* 2001;16:37–41.
55. Weissenborn K, Heidenreich S, Giewekemeyer K, Ruckert N, Hecker H. Memory function in early hepatic encephalopathy. *J Hepatol 2003;39:320–5*.

56. Prevalence And Natural History Of Subclinical Hepatic Encephalopathy In Cirrhosis Ananya Das, Radha K Dhiman Et Al *Journal Of Gastroenterology And Hepatology* (2001) 16, 531–535
57. Jalan r, Shawcross D, Davies n. The molecular pathogenesis of hepatic encephalopathy. *Int J biochem Cell biol 2003;35: 1175–1181*.
58. Lockwood AH, Yape W, Wong WH. Cerebral ammonia metabolism in patients with severe liver disease and minimal hepatic encephalopathy. *J Cereb blood Flow metab 1991; 11: 337–341.*
59. Das K, Singh P, Chawla Y, Duseja A, Dhiman RK, Suri S. Magnetic resonance imaging of brain in patients with cirrhotic and non-cirrhotic portal hypertension*. Dig Dis Sci 2008; 53: 2793–2798*
60. Rama Rao KV, Reddy PV, Hazell AS, Norenberg MD. Manganese induces cell swelling in cultured astrocytes. *Neurotoxicology 2007; 28:807–812*
61. Amodio P, Valenti P, Del Piccolo F et al. P300 latency for the diagnosis of minimal hepatic encephalopathy: evidence that spectral EEG analysis and psychometric tests are enough. *Dig. Liver. Dis. 2005; 37: 861–8.*
62. Sharma P, Sharma BC, Puri V, Sarin SK. Critical flicker frequency: diagnostic tool for minimal hepatic encephalopathy. *J. Hepatol. 2007; 47: 67–73.*

63. Romero-Gómez M, Córdoba J, Jover R *et al*. Value of the critical flicker frequency in patients with minimal hepatic encephalopathy. *Hepatology* 2007; 45: 879–85.
64. Rose C, Butterworth RF, Zayed J et al. Manganese deposition in basal ganglia structures results from both portal-systemic shunting and liver dysfunction. *Gastroenterology 1999; 117: 640–4.*
65. Yadav SK, Srivastava A, Srivastava A et al. Encephalopathy assessment in children with extra-hepatic portal vein obstruction with MR, psychometry and critical flicker frequency. *J. Hepatol. 2010; 216: 683–91.*
66. Sarin SK, Agarwal SR. Extra hepatic portal vein obstruction. *Semin liver disease*. 2002; 22:43-58
67. Cerebral oedema in minimal hepatic encephalopathy due to extra hepatic portal venous obstruction Amit Goel, Santosh Yadav et al - *Liver International (2010)*
68. Lactulose for minimal hepatic encephalopathy in patients with extra hepatic portal vein obstruction. Sharma P[1], Sharma BC. *Saudi J Gastroenterol. 2012 May-Jun;18(3):168-72.*

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CONTROLS

S. No	Name	AGE	SEX	NCT-A	NCT-B	NCT-T	DST	SDT	LTT	CFF
1	DHANAM	8	F	29	86	60	159	60	60	49
2	KARTHIK	8	M	88	105	132	193	58	89	47
3	SHWETHA	10	F	38	85	84	117	46	41	46
4	JEBASTIN	10	M	78	150	93	170	50	77	48.5
5	TAMILSELVI	11	F	32	93	71	148	35	45	48.5
6	NIBEN	11	M	52	70	78	167	63	60	48.5
7	SARASWATH	12	F	28	56	99	143	40	49	47
8	BHAVANI	11	F	45	52	77	122	50	46	46
9	LOHITHA	11	F	37	33	23	138	61	63	47
10	VINODHINI	11	F	52	113	43	100	55	60	48.5
11	GOPIKA	11	F	64	85	125	165	57	57	48.5
12	KIRAN	11	M	71	99	63	135	63	61	48.5
13	HISHTALAKS	10	F	47	77	131	157	47	50	47
14	JENISHA	12	F	24	38	17	106	29	48	48.5
15	SWARNA	13	F	29	49	51	131	37	41	48.5
16	KAVYA	13	F	28	55	37	130	31	37	48.5
17	MOHAMMEI	9	M	80	95	95	140	51	69	48.5
18	JEBARAJ	9	M	79	113	95	149	45	68	49
19	DELEIYA	10	F	42	91	73	127	56	53	49
20	BENNY	9	M	25	79	73	143	43	67	49
21	OGESHWAI	11	F	54	76	80	160	41	41	49
22	HARUMATH	11	F	28	48	56	142	42	50	49
23	JANANI	12	F	39	78	32	119	34	53	49
24	SUDHARNA	12	F	23	53	27	119	37	49	49
25	PARVEEN	12	F	22	37	43	134	38	48	47
26	YOGESH	10	M	57	97	93	156	55	48	46
27	BHANU	10	F	58	92	76	137	48	49	49.5
28	BINDHU	9	F	61	95	87	140	46	68	49.5
29	SARAVANAN	11	M	48	74	68	141	51	53	46
30	MANI	12	M	27	52	43	124	34	49	46.5

CASES

S. No	Name	AGE	SEX	Diagnosis	e at Diagnosodes of bl		OF PRESEN	ears since diagnosi	since first	HB	BILIRUBIN	AST
1	MYTHILI	8	F	Unknown	8	0	OMINAL M	0	0	10.4	0.8	23
2	ANBUMANI	8	M	Omphalitis	5	2	RICEAL BLE	3	3	9.8	0.9	28
3	DIANA	10	F	Unknown	5	1	OMINAL M	5	1	11.6	0.8	23
4	RISH KUM	10	M	Unknown	5	1	FEVER	5	1	10.8	0.8	29
5	OGESHWAI	11	F	Unknown	7	1	RICEAL BLE	4	7	12	0.6	28
6	THOMAS	11	M	Unknown	11	1	RICEAL BLE	0	0.5	8.9	0.8	34
7	MENAKA	12	F	Omphalitis	10	2	RICEAL BLE	2	2	10.7	0.8	33
8	ABITHA	12	F	Unknown	8	1	ANAEMIA	4	0.5	9.2	0.7	29
9	VANAJA	11	f	Unknown	8	2	RICEAL BLE	3	3	11	0.8	24
10	ARMILA BA	12	F	Unknown	9	1	RICEAL BLE	3	3	12	0.9	33
11	SAMUEL	9	M	Unknown	6	2	RICEAL BLE	3	3	12	0.8	23
12	BALAJI	10	M	Omphalitis	5	1	RICEAL BLE	5	5	10	1.1	23
13	GOVARDHAI	12	M	Unknown	12	1	RICEAL BLE	0	0.5	11	1	22
14	PRIYANKA	10	F	Unknown	10	1	RICEAL BLE	0	0.25	9.8	1	22
15	DIKSHITHA	11	F	Omphalitis	4	6	RICEAL BLE	7	7	11	1	32
16	NANDINI	11	F	Unknown	3.5	1	RICEAL BLE	7.5	3	8.9	0.9	32
17	NIRANJANA	9	F	Unknown	1.5	1	RICEAL BLE	7.7	7.5	9.8	0.7	26
18	DILLI RANI	11	F	Unknown	2	2	RICEAL BLE	9	2	10	0.9	30
19	KANNAN	12	M	Unknown	6	3	OMINAL M	6	6	11	0.7	30
20	RMAL KUM	11	M	Omphalitis	7	2	RICEAL BLE	4	4	10.2	1.2	23
21	DHINA	10	M	Unknown	1	10	RICEAL BLE	9	9	8.9	0.8	32
22	SOWMYA	11	F	Unknown	7	1	RICEAL BLE	4	6	11	0.7	30
23	PRIYANKA	13	F	Unknown	8	1	RICEAL BLE	5	0.5	10.4	0.8	28
24	YUVARAJ	9	M	Unknown	6	1	RICEAL BLE	3	1.5	10.8	1.1	26
25	HARIHARAN	10	M	Unknown	5	1	RICEAL BLE	5	1	10.6	1	23
26	SARAVANAN	9	M	Unknown	6	2	RICEAL BLE	3	3	10.2	0.7	30
27	MONIKA	12	F	Omphalitis	10	2	RICEAL BLE	2	2	11	0.9	28
28	SEETHA	11	F	Unknown	2	2	OMINAL M	9	2	9.8	0.9	30
29	PAVITHRA	13	F	Unknown	8	1	OMINAL M	5	0.5	11	1	28
30	VANAJA	11	F	Unknown	8	2	RICEAL BLE	3	3	11.4	0.8	33

ALT	ALBUMIN	OGD	Endotherap	Ht	Wt	BMI	NCT-A	NCT-B	NCT-T	DST	SDT	LTT	CFF Value
30	3.6	LV	0	120	20	13.89	73	159	161	319	61	73	45.5
21	3.6	LV+GV	10	128	23	14.02	70	119	151	208	58	61	45
33	3.7	LV	9	128	19.5	11.89	87	169	92	216	55	75	45.5
23	3.5	LV	15	125	20	12.82	114	313	158	445	95	99	44.5
28	3.4	LV	17	138	28	14.74	78	278	121	274	52	50	46.5
31	3.6	SV	4	141	29.5	14.9	36	97	60	153	49	79	47
23	3.8	LV	9	129	20.5	12.35	35	121	71	135	49	70	46.5
29	3.6	SV	9	132	24	13.79	50	70	89	202	53	71`	46
31	3.8	LV	0	136	26.3	14.29	46	86	60	158	49	45	47
33	3.5	SV	11	140	35	17.86	28	72	53	143	48	53	47
30	3.8	LV+GV	5	123	20.5	13.58	79	200	155	326	64	118	45.5
28	3.8	LV	14	124	18.5	12.01	136	132	109	295	70	78	45
31	3.5	SV	4	140	26	13.27	97	210	200	242	46	92	44.5
36	3.8	LV	0	126	24	15.19	140	199	200	420	49	86	45
21	3.6	LV+GV	20	131	24	14.04	113	107	109	304	40	80	48
32	3.6	LV	17	135	28	15.38	56	115	37	154	43	63	47.5
31	3.4	LV	16	127	22	13.67	63	133	89	188	48	75	47
31	3.5	LV+GV	19	140	27	13.78	48	164	112	166	38	61	45
30	3.9	LV	14	153	37.5	16.03	71	106	107	235	44	50	48
23	3.5	LV	17	133	26.5	14.97	85	108	82	222	48	66	47.5
18	3.5	LV	7	132	23	13.21	89	152	89	239	44	88	44
26	3.4	LV	23	136	26.3	14.21	52	46	67	180	39	54	46
30	3.4	SV	9	133	25	14.12	47	78	67	171	49	72	48
32	3.7	LV	22	123	23	15.23	144	257	177	283	61	51	44.5
26	3.8	LV	15	125	21	13.46	118	319	160	438	98	97	44
23	3.4	LV+GV	5	123	20.5	13.56	79	200	155	326	64	118	45
19	3.8	LV	9	129	20.5	12.41	38	124	76	138	51	71	48
28	3.8	SV	19	140	27	13.78	49	166	114	169	39	63	44.5
28	3.7	LV+GV	9	133	25	14.12	49	79	69	172	51	71	47
22	3.9	LV	0	136	26.3	14.21	47	87	61	159	51	46	46

ACRONYMS & ABBREVIATIONS

EHPVO – Extra Hepatic Portal Vein Obstruction

HE – Hepatic Encephalopathy

MHE – Minimal Hepatic Encephalopathy

PHT – Portal Hypertension

NSAID – Non-Steroidal Anti-Inflammatory Drugs

MRI – Magnetic Resonance Imaging

CHESS – Clinical Hepatic Encephalopathy Staging Scale

WAIS – Wechsler Adult Intelligence Scale

NCT-A – Number Connection Test-A

NCT-B – Number connection Test-B

NCT-C – Number Connection Test-Tamil

SDT – Serial Dotting Test

DST – Digit Symbol Test

LTT – Line Tracing Test

GI – Gastro-Intestinal

UGI – Upper Gastrointestinal

IGF – Insulin-like Growth Factor

IGFBP – Insulin-like Growth Factor Binding Protein

PROFORMA

Minimal Hepatic Encephalopathy in Children with EHPVO

Date:

Name: Age/Sex:

Standard/School: Medium:

Address: SE status:

Phone Number: Immunisation Status:

Diagnosis:

Aetiology of EHPVO: Omphalitis / Umblical Cannulation / abd. Sx / Trauma/ Recurrent Diarrhoea / Unknown

Age at Diagnosis:

History of UGI Bleed:

No. of episodes:

First Bleed:

Last Bleed:

History of Endo-therapy:

Drug History:

O/E:

Ht: Wt: BMI:

P/A:

LFT:

Viral Markers:

USG:

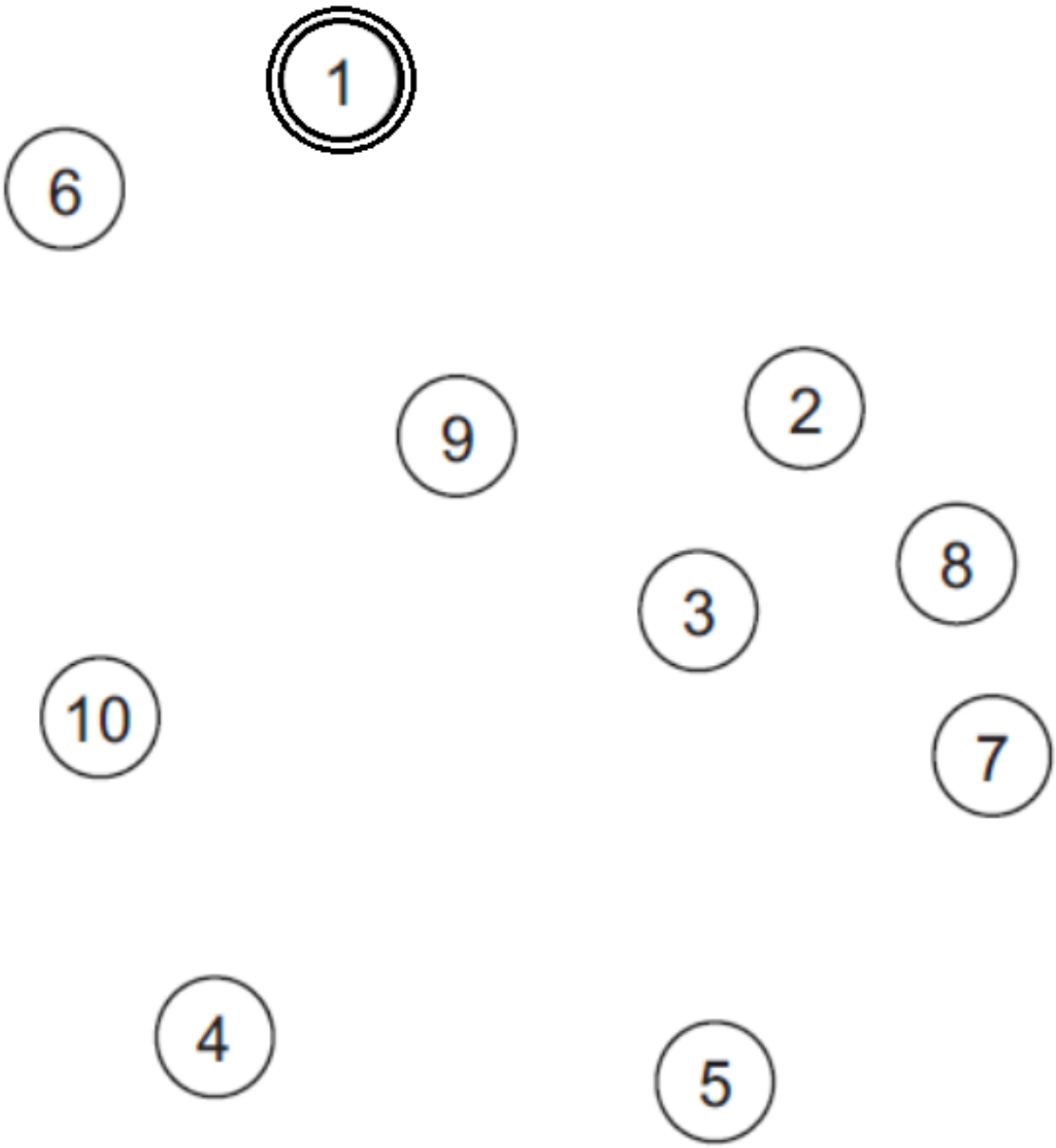
Doppler/CT Angio/MR angio:

Collaterals:

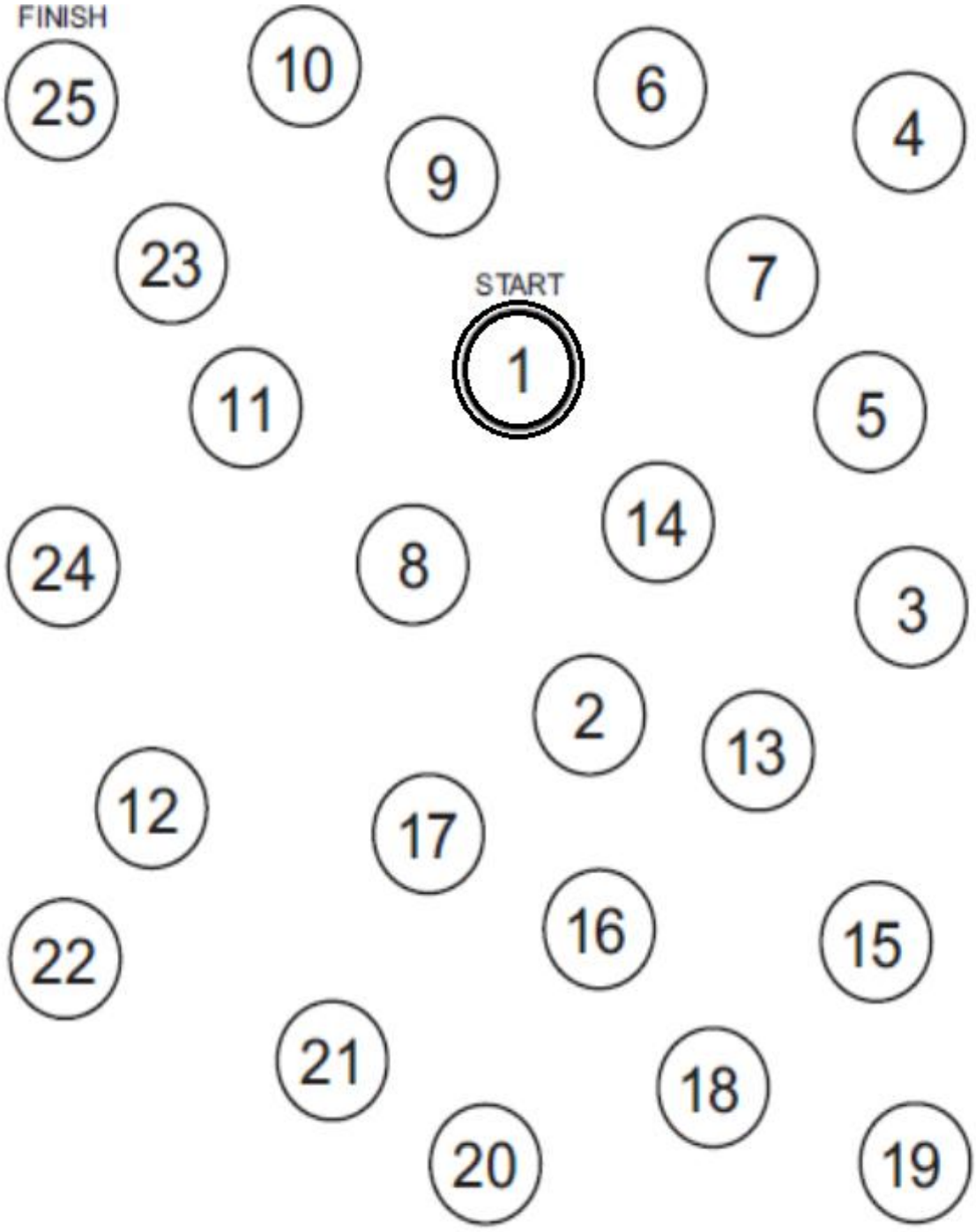
OGD:

Critical Flicker Frequency:

Number Connecion Test A - Sample

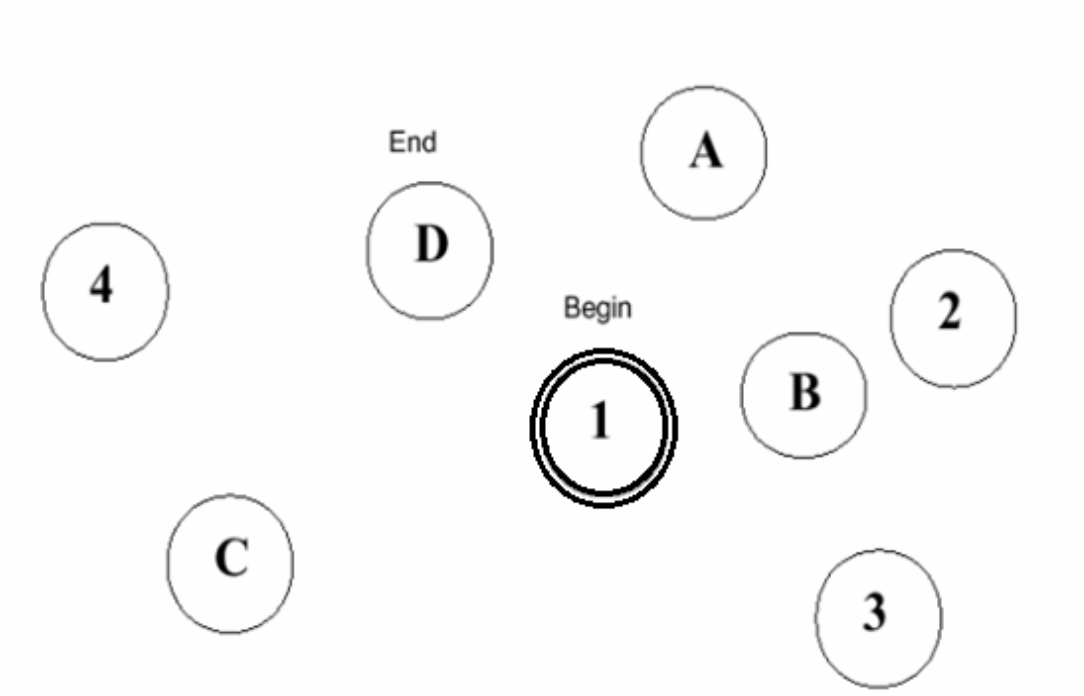


Number Connection Test- A

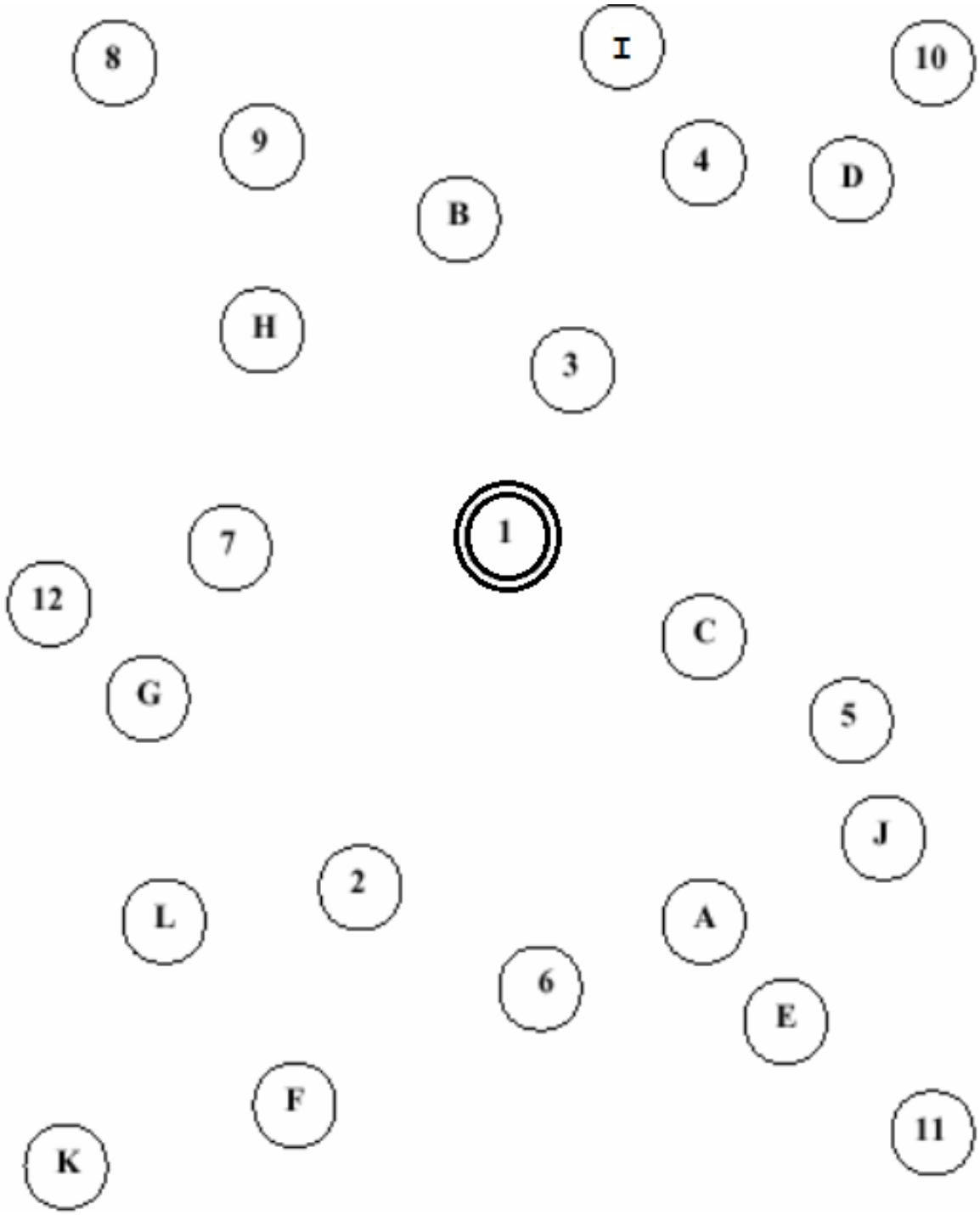


Score:

Number Connection Test B - Sample

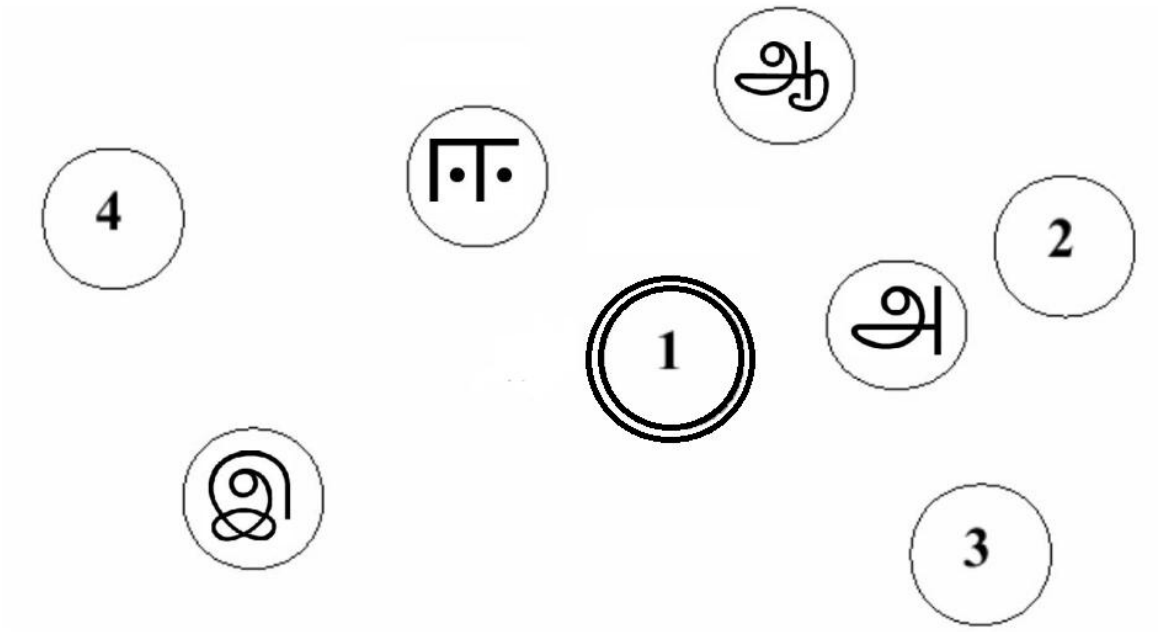


Number Connection Test –B

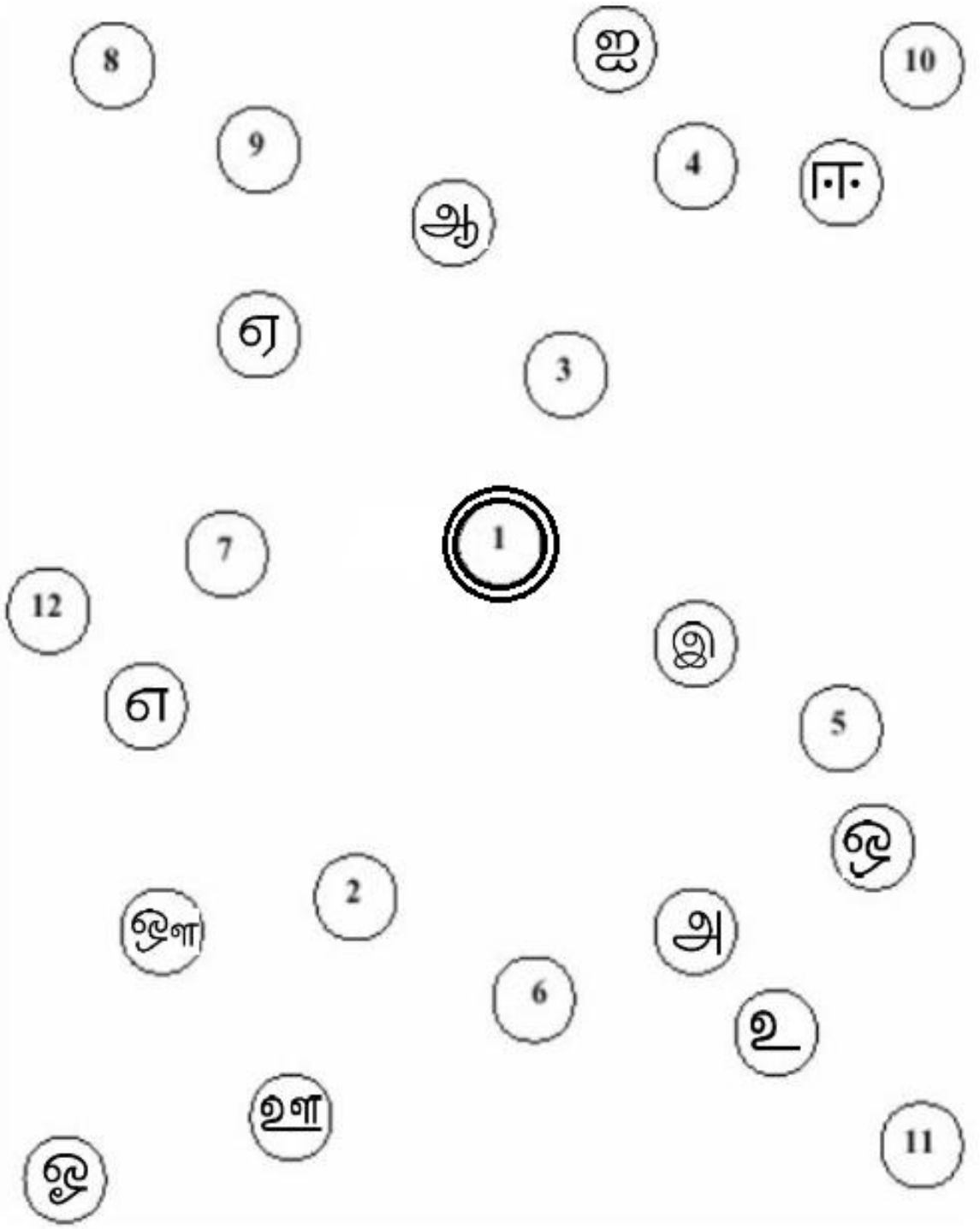


Score:

Number connection Test B- Tamil Sample



Number Connection Test B – Tamil



Score:

Digit Symbol Test

Digit	1	2	3	4	5	6	7	8	9
Symbol	—	†	Π	L	Γ	o	∧	X	=

Example

Digit	1	3	7	2	4	8	2	1	3	2	1	4	2	3	5	2	3	1	4	5	6	3	1
Symbol	—	Π	∧	†	L	x																	

Digit	4	5	4	2	7	6	3	5	7	2	8	5	4	6	3	7	2	8	1	9	5	8	4
Symbol																							

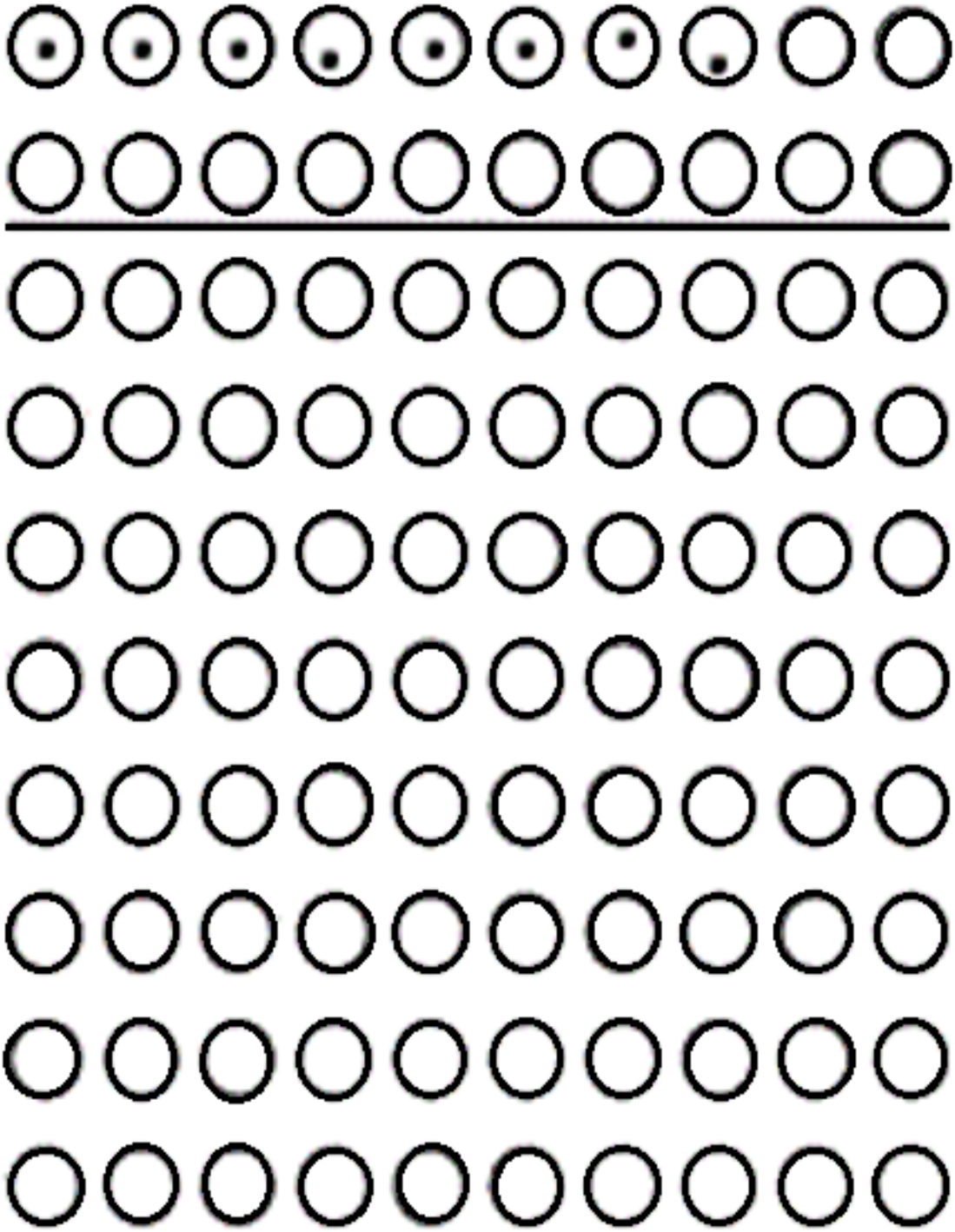
Digit	7	3	2	8	1	7	9	4	6	8	5	9	7	1	8	5	2	9	4	8	6	3	7
Symbol																							

Digit	1	3	7	2	4	8	2	1	3	2	1	4	2	3	5	2	3	1	4	5	6	3	1
Symbol																							

Digit	4	5	4	2	7	6	3	5	7	2	8	5	4	6	3	7	2	8	1	9	5	8	4
Symbol																							

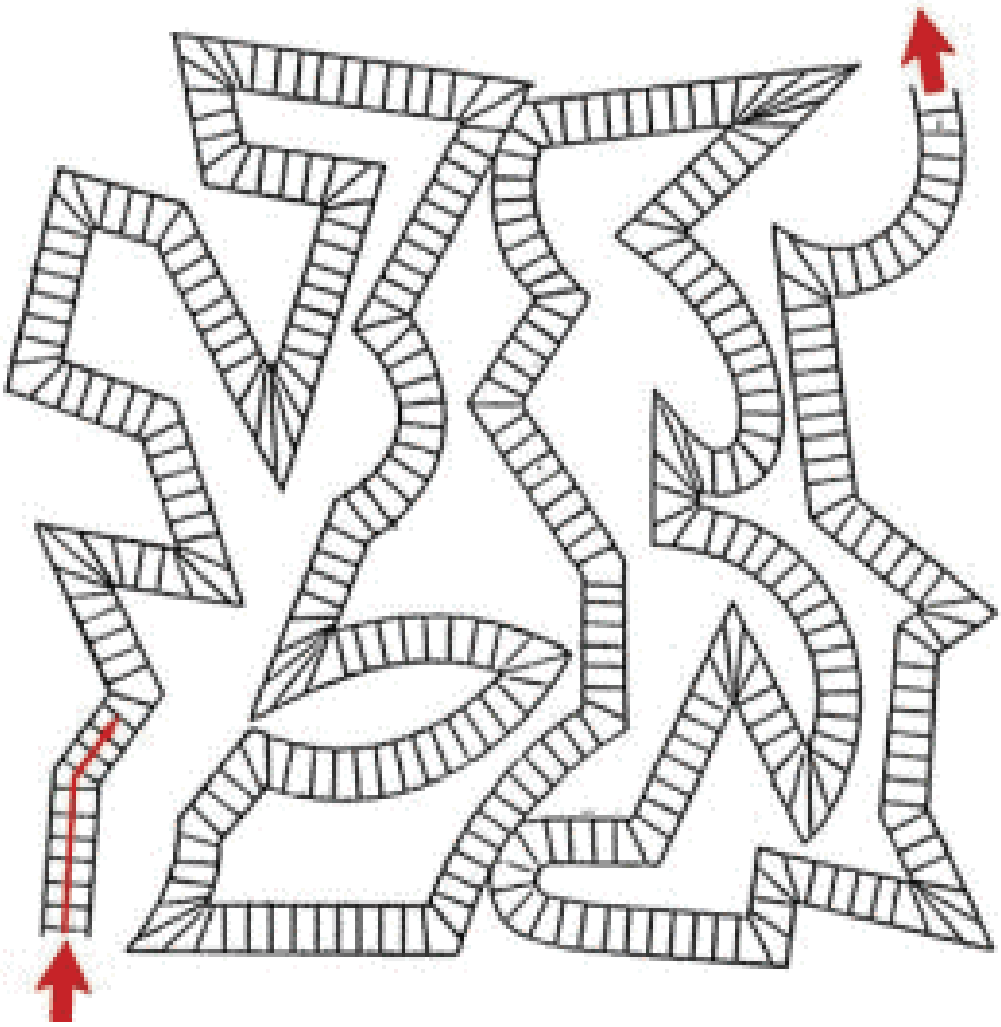
Score:

Serial Dotting Test



Score:

Line Tracing Test



Time Score:
Error Score:
Total Score:

Information Sheet and Consent

We are conducting a study on "Hepatic Encephalopathy in Children with Extra-Hepatic Vein Obstruction", at The Department of Medical Gastroenterology – Rajiv Gandhi Government General Hospital, Chennai and Institute of Child Health, Chennai. The purpose of this research is to study the prevalence of Minimal Hepatic Encephalopathy in school children with Extra-Hepatic Portal Vein Obstruction and when present, to assess its relation to the extent of Porto-systemic collaterals.

The privacy of your child in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide on whether your child participates in this study and are fee to withdraw him/her from this study at any time. Your decision will not result in any loss of benefits to which your child may otherwise be entitled.

The results of the study may be intimated to you at the end of the study period or during the study if anything is found abnormal. This may aid in your child's management and treatment.

Signature of the Investigator Signature of the Parent/Guardian

ஆராய்ச்சி தகவல் தாள்

சென்னை இராஜீவ்காந்தி அரசு பொது மருத்துவமனை மற்றும் அரசு குழந்தைகள் நல மருத்துவமனைக்கு வரும் பிள்ளைகளின் கல்லீரல் நோயினால் பாதிக்கப்பட்டவர்கள் குறித்த ஆய்வு இங்கு நடைபெற்று வருகிறது.

உங்கள் பிள்ளையும் இந்த ஆராய்ச்சியில் பங்கேற்க விரும்புகிறோம். இந்த ஆராய்ச்சியில் பங்கேற்க வைத்து அதன் தகவல்களை ஆராய்வோம். அதனால், உங்கள் பிள்ளையின் நோயின் ஆய்வறிக்கையோ, சிகிச்சையோ பாதிக்கப்படாது என்பதைத் தெரிவித்துக் கொள்கிறோம்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போதோ அல்லது ஆராய்ச்சின்போதோ தங்கள் பிள்ளையின் பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம்

பங்கேற்பாளர் கையொப்பம்

பங்கேற்பாளரின் உறவினர் கையொப்பம்

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு

"கல்லீரல் நோயினால் பாதிக்கப்பட்டவர்களைப் பற்றிய ஆய்வு"

ஆராய்ச்சி நிலையம் : இராஜீவ்காந்தி அரசு பொது மருத்துவமனை சென்னை மருத்துவக்கல்லூரி மற்றும் அரசு குழந்தைகள் நல மருத்துவமனை, எழும்பூர், சென்னை - 600 008.

பங்கு பெறுபவரின் பெயர் :

பங்குபெறுபவரின் எண் :

பெற்றோரின் பெயர் :

பங்கு பெறுவர் இதனை (✓) குறிக்கவும்.

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நானும் என் பிள்ளையும் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறோம். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நாங்கள் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தகமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என் பிள்ளையின் மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக்கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் என் பிள்ளை பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். ☐

இந்த ஆய்வில் என் பிள்ளைக்கு இரத்தம், வயிறு ஸ்கேன், உள்நோக்கி பரிசோதனை மற்றும் க்ரிடிக்கல் பிளிக்கர் பரிசோதனை செய்துகொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் ..... இடம் ..... தேதி

கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம் ..... தேதி

ஆய்வாளரின் பெயர் .....

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. K. Raja Yogesh,
PG in DM Medical Gastroenterology,
Department of Gastroenterology,
Madras Medical College,
Chennai-3.

Dear Dr. K. Raja Yogesh,

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled **"Minimal Hepatic Encephalopathy in Children with Extra-Hepatic Portal Vein Obstruction"** No. 37092013

The following members of Ethics Committee were present in the meeting held on 10.09.2013 conducted at Madras Medical College, Chennai-3.

1. Dr. G. Sivakumar, MS FICS FAIS	-- Chairperson
2. Prof. R. Nandini, MD Director, Instt. of Pharmacology, MMC, Ch-3	-- Member Secretary
3. Prof. Shyamraj, MD Director i/c, Instt. of Biochemsitry, MMC, Ch-3	-- Member
4. Prof. P. Karkuzhali, MD Prof. Instt. of Pathology, MMC, Ch-3	-- Member
5. Prof. Kalai Selvi, MD Prof. of Pharmacology, MMC, Ch-3	-- Member
6. Prof. Siva Subramanian, MD Director, Instt. of Internal Medicine, MMC, Ch-3	-- Member
7. Thiru. S. Govindasamy, BABL	-- Lawyer
8. Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

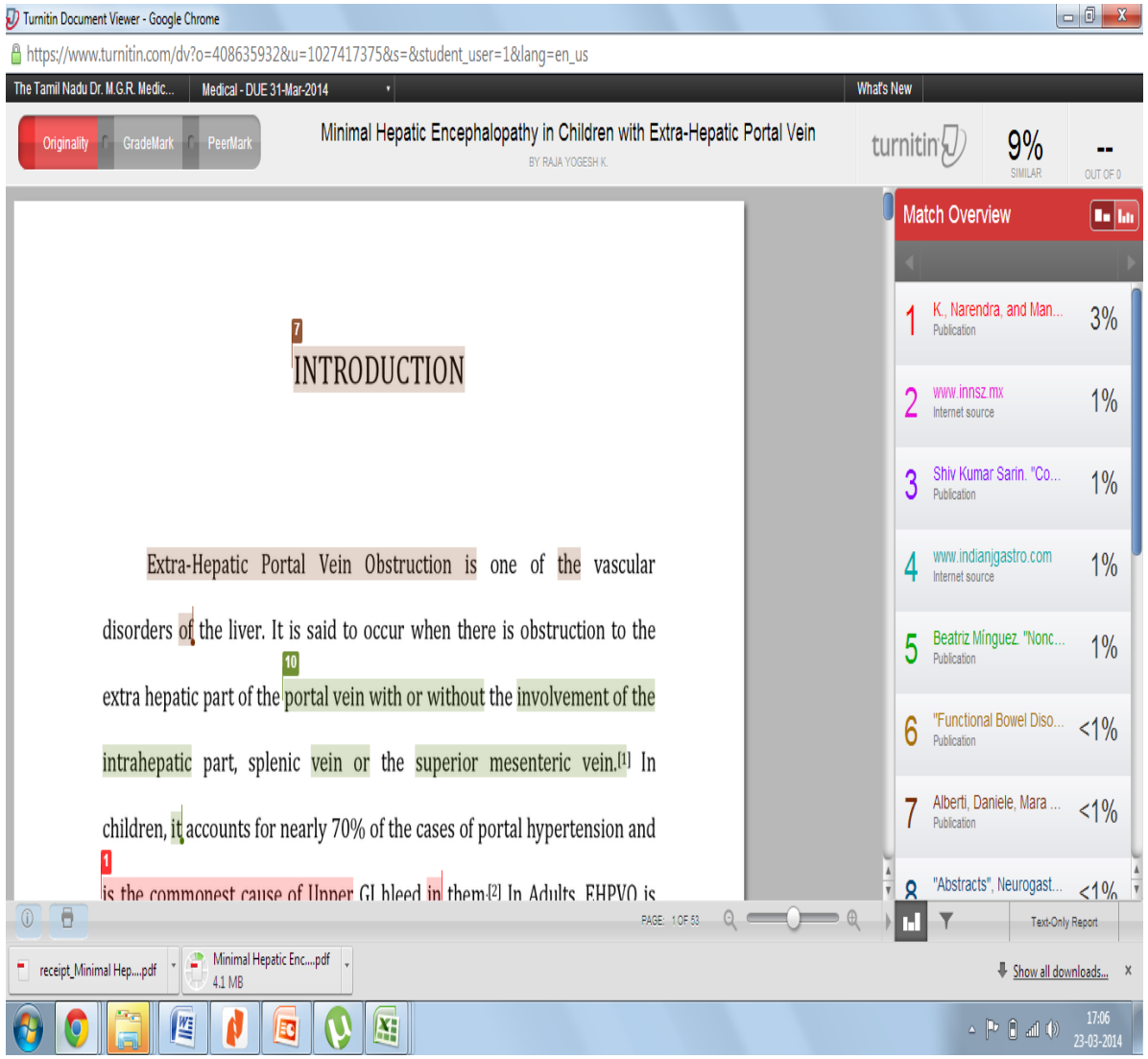
Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

13/3/13

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003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INTRODUCTION
Extra-Hepatic Portal Vein Obstruction is one of the vascular disorders of the liver. It is said to occur when there is obstruction to the extra hepatic part of the portal vein with or without the involvement of the intrahepatic part, splenic vein or the superior mesenteric vein.[1] In children, it accounts for nearly 70% of the cases of portal hypertension and is the commonest cause of Upper GI bleed in them.[2] In Adults, EHPVO is
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INTRODUCTION

Extra-Hepatic Portal Vein Obstruction is one of the vascular disorders of the liver. It is said to occur when there is obstruction to the extra hepatic part of the portal vein with or without the involvement of the intrahepatic part, splenic vein or the superior mesenteric vein.[1] In children, it accounts for nearly 70% of the cases of portal hypertension and is the commonest cause of Upper GI bleed in them.[1] In Adults, EHPVO is responsible for nearly one-third of cases of portal hypertension.[2]

Etiologically, EHPVO is a heterogeneous disease and the cause varies