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Evaluation of Nutritional Status of Hospitalized Infants with Cholestatic Jaundice in a Tertiary Care Center in Bangladesh

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Abstract

Introduction: *Nutritional management becomes crucial for the infants of cholestatic jaundice as they suffer from impaired digestion and absorption of fatty acid and fat soluble vitamins. Thus evaluation of nutritional status was done to identify undergoing malnutrition.* ***Materials and Methods:*** *It was a cross-sectional, prospective study done in the indoor patients department of paediatric gastroenterology and nutrition, BSMMU; since April 2016 to September 2016 (6 months). Purposive sampling was done from the infants (2 weeks to 12 months age) with cholestatic jaundice or having neonatal jaundice persisting more than 2 weeks. Linear regression analysis was done for correlation between different anthropometric variables.* ***Results:*** *Total 47 patients were enrolled in this study although 93 patients were admitted with cholestatic jaundice in that time period in the department. Most of them were found biliary atresia (61.70%) Idiopathic Neonatal Hepatitis (31.91%). Among anthropometric indices, Weight for length Z(WLZ) Score mean was -1.6 (±1.6), Triceps skin fold thickness (TST) mean 5.48 (±2.75) mm, and Subscapular skin fold thickness(SST) mean was 4.13 (±2.39)mm. Linear regression analysis of each variables done with other and found positive correlation between TST with WLZ Score and SST with WLZ score and found highly significant (p=0.008 in ANOVA) and (p=0.011 in ANOVA) respectively.* ***Conclusion:*** *Cholestatic babies were found mild to moderately malnourished in our study. Skin fold thickness was found to be an important early clinical marker for diagnosis of malnutrition which was found positively correlated with the standard procedure of anthropometry in our study.*

Key words: *Cholestatic jaundice, Nutritional status, Biliary atresia, Neonatal hepatitis.*

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Introduction:

Jaundice is a clinical sign characterized by yellowish discoloration of skin and mucous membrane caused by elevated serum bilirubin concentration. Elevated conjugated or direct bilirubin in serum >20% of total serum bilirubin is one of the important biochemical markers of cholestasis indicating perturbation of bile flow [1,2]. Conjugated hyperbilirubinemia is less common, affecting approximately 1 in 2,500 infants [3,4,5] and biliary atresia is one of the important causes of cholestasis occurring in between 1 in 10,000 to 1 in 20,000 infants[6]. In India it constitutes 19% to 33% of all chronic liver diseases in children reporting to tertiary care hospitals[7]. Early recognition of cholestasis is essential for effective treatment of medical condition or the surgical management of biliary anomalies, even when treatment is not yet available or effective, infants who have progressive liver disease can be benefited from optimal nutritional support and medical management of the complications of cholestasis and possibly cirrhosis [8].

The consequences of prolonged cholestasis are profound, resulting in malabsorption, failure to thrive, and deficiencies of fat-soluble vitamins like A, D, E, K and various minerals like Calcium, Phosphate and Zinc. Cholestatic babies are at special risk for life-threatening bleeding due to vitamin K deficiency. These babies need more calories (130% more than RDA) to maintain growth and also nutritional supplementation at diagnosis and thereafter. Very few studies found in Bangladesh as well as in other parts of the world regarding the nutritional status of infants with cholestatic jaundice. Routine measurements of anthropometry like stunting or wasting can be a good marker of chronic nutritional deprivation. In Bangladesh, 36 % among all children under 5 are considered to be

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short for their age or stunted, while 12 % are severely stunted (below -3 SD). The prevalence of stunting increases with age from 14% of children under age 6 months to 46 % of children 18-23 months and decreases to 38% among children 48-59 months[9]. Thus, study was conducted to indentify the nutritional status of the study subjects and quantify them among other parameters for correlation so that we could manage accordingly.

Materials and Methods:

It was a prospective cross-sectional study done in the indoor patients Department of Paediatric Gastroenterology and Nutrition, BSMMU since April 2016 to September 2016 (Six months after approval of protocol) among the children admitted between ages 2 weeks -12 months with cholestatic jaundice. There were 93 patients admitted with cholestatic jaundice during study period and among them 47 were enrolled in the study. Inclusion criteria were Infants (2 weeks to 12 months age) with cholestatic jaundice (S. conjugated bilirubin > 2 mg or more than 20% of total serum bilirubin) or Neonatal jaundice persisting more than 2 weeks. Patients with age less than 2 weeks or more than 12 months, jaundice due to other causes, seriously ill infants who need referral or whose parents refused to be enrolled in the study were excluded. Sample selection was done by purposive sampling; interview was taken after written informed consent. Data were collected and put in the structured questionnaire then tabulated for analysis. A detailed history was obtained from mother or informant of infants with cholestatic jaundice (scleral icterus, dark urine and pale stool) persisting beyond 2 weeks of postnatal age and recorded in a predesigned questionnaire. A thorough physical examination, including examination of the eyes, stool color was observed daily after admission to look for persistent or intermittent nature of icterus and pale stool and examination findings were recorded. Anthropometric measurement (Weight, Length, MUAC, Triceps skin fold thickness, Sub-scapular skin fold thickness) was taken by standard routine procedure. Weight was measured by electronic baby weighing scale in kilogram and gram, Length was measured by Infantometer in centimeter, Mid Upper Arm Circumference (MUAC) was measured by Shakir's Tape in millimeter, measurement of Triceps & Sub-scapular skin fold thickness was done by Harpenden calipers in millimeter. After measurement, each data was compared with 'WHO Child Growth Standards' published by Center for Disease Control and Prevention, November 1, 2009. Complete blood count and liver function tests (S. bilirubin - total & direct, ALT, ALP, and PT) was done. Urine was tested for non-glucose reducing substances. Ultrasonography of the hepatobiliary system, and Hepatobiliary scintigraphy was done. In scintigraphy, absence of radioactivity in the small bowel after 24 hours was considered as absent tracer excretion. Data were processed and analyzed using SPSS (Statistical Package for Social Sciences) software version 16. Continuous scale data were presented as mean, standard deviation, range and Categorical data were presented as number percentage. The summarized data were present in the table and chart. All the participants were volunteered. Informed written consent was taken from all patients' guardian. All documents were preserved confidentially. Questions were asked in Bangla and also in local easily understandable language.

Results:

Anthropometric measurements showed mean weight (n=47) was 4651.48 (±1456.36) grams, mean length (n=47) was 57.36 (±3.93) cm, mean MUAC(n=7) was 112.50(±7.50) mm, Triceps Skin fold Thickness(TST) (n= 23) 5.48 (±2.75) mm and TST Z score mean (n=23) was -2.83 (±2.21) , Sub-scapular Skin fold Thickness(SST) (n=23) 4.13(±2.39) mm and SST Z score mean was (n=47) -3.26 (±2.62). Weight for age Z score (WAZ) mean was -2.51 (±1.59) (n=47) , length for age Z score (LAZ) mean was-1.92 (±1.49) (n=47) and weight for length Z score mean was -1.61 (±1.60) (n=47). Linear regression analysis of each variables done with other and found positive correlation between Triceps skin fold thickness with Weight for length Z Score and it was highly significant (p=0.008 in ANOVA). Same positive correlation was found between Subscapular skin fold thickness with Weight for length Z Score, it was also statistically highly significant (p=0.011 in ANOVA). On the other hand Triceps and Subscapular skin fold thickness values were found positively correlated with Length for age Z score values but those were not statistically significant (p=0.097 and p=0.645 respectively). The following figures describes this scenario in details.

Figure 1 shows the correlation between Weight for Length Z score (Wasting) with Triceps Skin Fold Thickness (TST) Z score by Linear Regression Analysis which found a positive correlation between these variable and it was highly significant (p=0.008 in ANOVA).

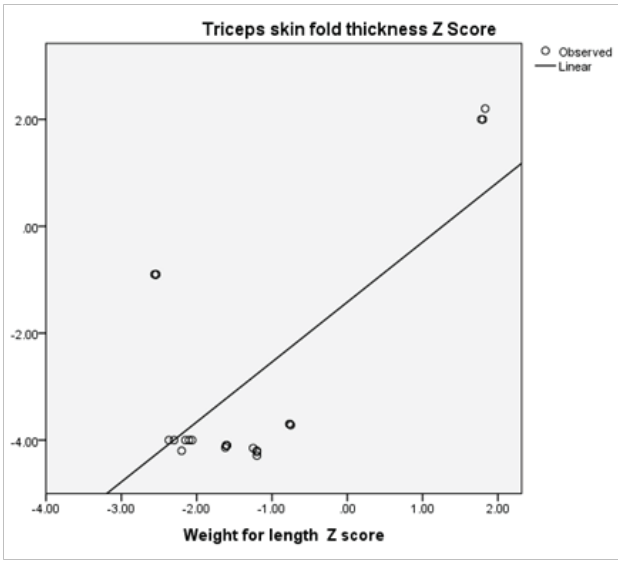

Figure-1: Linear Regression Analysis of Triceps Skin Fold Thickness Z score (TSTZ) and Weight for Length Z score (WLZ) correlation analysis.

Figure 2 shows the correlation between Weight for Length Z score (Wasting) with Subscapular Skin Fold Thickness (SST) Z score by Linear Regression Analysis which found a positive correlation between these variable and it was highly significant (p=0.011 in ANOVA).

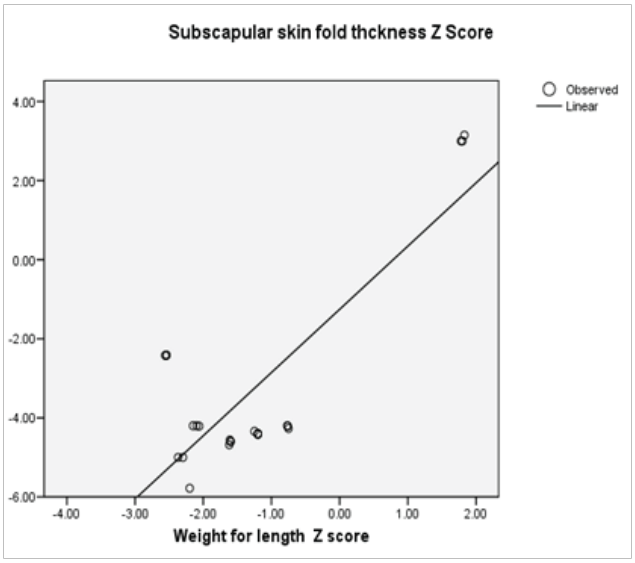

Figure-2: Linear Regression Analysis of Subscapular Skin Fold Thickness Z score (SSTZ) and Weight for Length Z score (LAZ) correlation analysis.

Discussion:

This study was done to evaluate the nutritional status of the cholestatic infants who were and we found most of them were severely underweight (44.7%), moderately stunted (46.8%) and mildly wasted (44.68%). This result indicates a quite high prevalence of stunting among cholestatic infants (87.2%) in respect to our national prevalence of stunting (14%) according to Bangladesh Demographic Health Survey 2014[9].

Present study showed the mean age was 3.19 (±1.67) months and minimum age was 1 month and maximum being 7 months. Hamid F, Afroza A and Ray P C [1] compared between Biliary Atresia(BA) group with Neonatal Hepatitis(NH) group and showed mean age of babies in BA group was 4.13 (± 2.11SD) months, where as in NH babies mean age was 3.86 (± 2.11SD) months. We found most of the patients were male 41 (87%), male female ratio 6.83:1 among them. Among cholestatic babies Biliary atresia has been reported to be common in female infants in several others previous studies. Where as, we found only 1 case out of 29 Biliary atresia cases is female. However, in Karim ASM B and Kamal M[11] series, 10 of 16 infants with BA were male (62.5%). This indicates a male preponderance in our region. Most of our study subjects came from rural (72.3%) low socioeconomic (57%) background where there is custom of giving more privilege to male child than female. There is also some difference we found in relation to initial diagnosis of the babies. Our study found BA in 29 (61.7%) cases and NH in 15 (31.91%) cases where as Hamid F, Afroza A and Ray P C [1] showed BA in 12 (40%) cases and NH 18 (60%) cases which is almost reverse picture of our study. Both the studies done in BSMMU but the difference may be due to the time of study, the former was done in 2007. In these long 9 years Paediatricians became more conscious about the surgical treatment option of BA cases in BSMMU and thus responded promptly in referral which was also reflected in our study subject's age of enrollment (72.34% before 3 months of age).

Silva F et al.[12] study done over 91 children with cholestasis, with current median age of 12 months. WAZ and HAZ indices below −2 Z-scores were observed in 33% and 30.8% of patients, respectively; where as in our study it was 57.44% and 59.57% respectively. Concerning the WLZ index and BMI, only 12% and 16% of patients, respectively, were below −2 Z-scores and in our study WLZ below -2 was 31.91%. Regarding Mid Upper Arm Circumference (MUAC), 43.8% of 89 evaluated patients had some depletion. Observing the Triceps Skin Thickness(TST), 64% of patients had depletion, and 71.1% of the 45 evaluated patients had some degree of depletion regarding the MUAC. They concluded as, the use of weight for nutritional evaluation may underestimate the detection of malnutrition in patients with chronic liver diseases due to visceromegaly, subclinical edema, and/or ascites. The anthropometric indices that consider weight and height, such as WLH and BMI, may also not reveal the real degree of depletion attributable to chronic clinical condition of these patients, in which both weight and height are impaired. TST and MUAC measures appear to be more accurate parameters for nutritional evaluation of patients with liver diseases and cholestasis. Our study found 36 infants out of 47 were malnourished (weight for length Z score below -1). We found most of them were severely underweight (44.7%), moderately stunted (46.8%) and mildly wasted (44.68%). This result indicates a quite high prevalence of stunting among cholestatic infants (87.2%) in respect to our national prevalence of stunting (14%) according to Bangladesh Demographic Health Survey 2014. Skin fold thickness also reflects the same picture. We could measure skin fold thickness in ≥3 months age group babies and found 23 study subjects and in those cases triceps and sub-scapular skin fold thickness Z-score mean was -2.83 (±2.21) and -3.26 (±2.62) respectively. If we consider the same gradation for skin fold thickness Z-score as we used for weight for length Z-score, this would indicate the babies were moderate to severely malnourished. Only 6(26%) out of 23 babies were found Z-score above -3 in both triceps and sub-scapular skin fold thickness measurement. Although several previous studies found MUAC as an important and relevant indicator of nutrition particularly in this age group, We found only 7 babies ≥6 months age group and MUAC was also measured in those babies and found mean 112.50 (±7.50) mm, all of them were in malnourished category including 4 babies in the category of severe acute malnutrition(SAM). This result strengthened our present study.

We have also done the analysis of correlation between Skin fold Thickness with Stunting and, Skin fold Thickness with

Wasting and found positive correlation in all aspects between these but degree of stunting was not significantly associated with degree of skin fold thickness Z score (TSTZ with LAZ p value was 0.097 and SSTZ with LAZ p value was 0.645) as shown in Figures. We have shown that TSTZ and SSTZ was highly significantly associated with Wasting that is WLZ (TSTZ with WLZ p value was 0.008 and SSTZ with WLZ p value was 0.011).

We also found cholestatic babies with anaemia, raised serum marker of parenchymal and biliary epithelial cell damage like raised Alanine Aminotransferase (ALT), raised Alkaline Phosphatase (ALP), raised Gamma-glutamyl transpeptidase (GGTP) and most importantly they had coagulopathy as reflected by raised PT. Their mean Haemoglobin was 9.60 (±2.32) gm/dl, mean total S. bilirubin was 11.31 (±3.66) mg/dl, mean Direct S. Bilirubin was 6.97(±3.39) mg/dl, mean S. ALT was 142.46 (±83.72) IU/L which was 3.2 times higher than upper limit normal value, mean GGTP was 333.76 (±263.35) IU/L which was 2.5 times higher than upper limit normal for any age, mean ALP was 695.48 (±855.04) IU/L and mean Prothombin Time (PT) was 36.53 (±39.95) seconds which was 2.25 times higher than upper limit normal value . Mattar et al[13] study showed mean ALP (U/l) 1,708 (938-2,020), GGTP (U/l) 216 (104-351), Total bilirubin (mg/dl) 9.6 (5-13.1), Direct bilirubin (mg/dl) 6.9 (4-11.6), Prothrombin activity (%) 77 (39-98). It has been reported that serum bilirubin rarely exceeds 12 mg/dL (and may be as low as 5-8 mg/dL) in infants with BA despite complete bile duct obstruction, whereas it may exceed 20 mg/dL in those with NH[11]. In the series by Karim ASM B and Kamal M[11], mean serum bilirubin was 10.4 mg/dL in infants with BA and 14.1 mg/dL in those with NH_2. Serum GGTP level was the only biochemical test found to be of discriminating value between hepatocellular Cholestasis and Biliary atresia. GGTP values less than 200 U/L correlated with the diagnosis of hepatocellular cholestasis while GGTP values more than 200 U/L favored the diagnosis of biliary atresia. However, our study did not correlated with such findings of GGTP. We did not find any cholestatic baby having non-glucose reducing substance in urine.

During Ultrasonography of hepatobiliary system we found 24 (51.1%) babies with abnormal findings like absent or non-contraction of gall bladder, hepatomegaly, splenomegaly, ascites. Hepatobiliary scintigraphy also done in all patients and found absent tracer activity in small intestine in 25 (53.2%) babies.

Suchy FJ[8] study proposed some nutritional interventions for cholestatic babies like: giving energy dense food which will fulfill 125-130% of RDA of the age group, giving Medium Chain Triglyceride (MCT) which does not require bile acid for absorption, adequate protein intake (2-3gm/kg/day in infants), giving vitamin A 5000-25000 U/d of water miscible preparation, Vitamin D 0.05-0.3 mcg/kg/day, Vitamin E d-alpha tocopherol polyethylene glycol-1000-succinate 15-25 u/kg/day, Vitamin K Phytomenadione 2.5-5 mg twice weekly up to 5 mg/day orally or Inj IM 2-5 mg every 4 weekly. Sokol RJ and Stall C[10] also recommends Calcium 50 mg/kg/day orally, Phosphate 25mg/kg/day orally , Zinc 1 mg/kg/day orally. Suchy FJ[8] also recommends that the diet of the cholestatic babies should be free of Copper, Aluminium and Manganese.

Conclusion:

Cholestasis is an important cause of growth failure in neonate and in early infancy which can be prevented by early identification and nutritional management. These babies were found mild to moderately malnourished in our study. Skin fold thickness is found to be correlated with the standard procedure of anthropometry for diagnosis of malnutrition at an early age.

Conflict of Interest: None.

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