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Comperative study of vitamin D levels in Haemophilia and healthy children

Abhishek Sanadhya[1], Jagdish Singh[2]
[1,2] *Department Of Paediatrics,Spmchi,J.K.Lon Hospital,S.M.S Medical College, Jaipur, Rajasthan*

Abstract
Objective: To compare the difference in serum vitamin D levels of pediatric haemophilic patients and healthy children
Study Design: Hospital based observational study conducted in dept . of paediatric medicine SPMCHI SMS medical college Jaipur on Haemophilia patients and healthy children.
Method: Vitamin D status was evaluated using laboratory test.
Results: significant correlation between severity of Hemophilia and Vitamin D insufficiency.
Conclusion: severe vitamin D deficiency may increase the risk of Hemophilic arthropathy and early supplymentation with Vitamin D may prevent severe joint disease in young Hemophilic children
Keywords: Serum vitamin D levels,Heamophilic patients,Healthy children

I. Objectives

Patients with hemophilia are at risk for developing reduced bone density in childhood and adolescence for number of reasons such as recurrent haemarthrosis and immobilization. Until recently, only few sports, such as golf and swimming, were recommended for patients with hemophilia. Despite liberalization of these recommendations, children with severe hemophilia are less likely to participate in weight-bearing, high-impact exercise. Patients with established changes of hemophilic arthropathy, characterized by pain, swelling, and joint instability, are even less likely to participate in sporting activities and may be at particular risk for reduced bone density. Finally, patients with Hemophilia who have been exposed to hepatitis C through infusion of contaminated plasma, clotting factor concentrates, or other blood substitutes may develop liver impairment and abnormalities in vitamin D metabolism and may be at risk of low bone density[2]. Patients with hemophilia and reduced bone mineral density (BMD) may be at increased risk of fractures and osteoporosis in later life. This study was conducted to compare the difference in serum vitamin D levels of pediatric haemophilic patients and healthy children and to assess the various factors with serum vitamin D severity levels in Haemophilia patients.

II. Methods

The study was conducted in the department of Pediatric Medicine, Sir Padampat Mother and Child Health Institute, S.M.S. Medical College, Jaipur from June 2014 to June 2015. It was a Hospital based Analytical Type of observational study ,whereSubjects divided in two groups:
A. Children affected with severe, moderate and mild Hemophilia A and Hemophilia B disease diagnosed by factor assay attended the OPD, Emergency or admitted in wards of SPMCHI, SMS Medical College
B. Non hemophilic matched controls
There were 80 subjects in each group. Assuming vitamin D deficiency in haemophilic children 63.6%{as per seed article}and 30 to 50% in general population aged 1 to 18 years [as per the reference article].Sample size is calculated 78 which is round of to 80 for study purpose with power of study being 80% and 0.05 alpha error

Inclusion Criteria
1. Confirmed cases of haemophilia of all types and all severity
2. Age from1 to 18 years.

Exclusion Criteria
1. Clinically relevant coagulation disorders other than hemophilia A & B
2. Those with other concomitant disease affecting vitamin D levels e.g. Chronic Kidney Disease, celiac disease and Malnutrition, (PEM Grade III, IV,)

III. Statistical Analyses

Statistical analyses were done using computer software (SPSS version 20 and primer). The qualitative data were expressed in proportion and percentages and the quantitative data expressed as mean and standard deviations. The difference in proportion was analysed by using chi square test and the difference in means were

analyzed by using student T Test .and Correlation analyses were performed using Pearson correlation coefficient .Significance level for tests were determined as 95% (P< 0.05). The subjects of both study group were selected as per the inclusion and exclusion criterion. Hemophilia affected children thus selected were evaluated in detail with regards to the age of onset of symptoms, mode of presentation, family history of bleeding/ hemophilia, severity of bleeding episodes and their relation to trauma , number of bleeding episodes with respect to time, most common site of bleeding, most common joint involved, therapies taken for bleeding episodes including blood products and / or factor concentrates, number of times therapy being taken, response to therapy, age of using blood product / factor for the first time.

- Records were evaluated for age at diagnosis, factor VIII or factor IX levels at the time of diagnosis, treatment received.

The patients were classified into Hemophilia A and Hemophilia B depending upon Factor VIII and Factor IX levels. Further classification into Severe, Moderate and Mild Hemophilia A and B was done on the basis of factor VIII or Factor IX levels at the time of diagnosis.

Serum vitamin D level will be done by chemeluminescene method after having fresh blood sample from the cases vitamin D is stable compound its level will not be affected by time lag between sample collection and sample processing

Anthropometery and Serum Calcium, s. phosphorus and Serum Alakaline phosphatese, Renal Function Test, Liver Function Test will be done to screen for other common diseases causing fluctuation in Vitamin D levels.

6. According to Most Studies Serum Vitamin D Levels in Haemophlic children are classified as

>30 ng mL^{-1} (normal)	**21–29 ng mL^{-1} (relative insufficiency)**	**<20 ng mL^{-1} (severe insufficiency)**

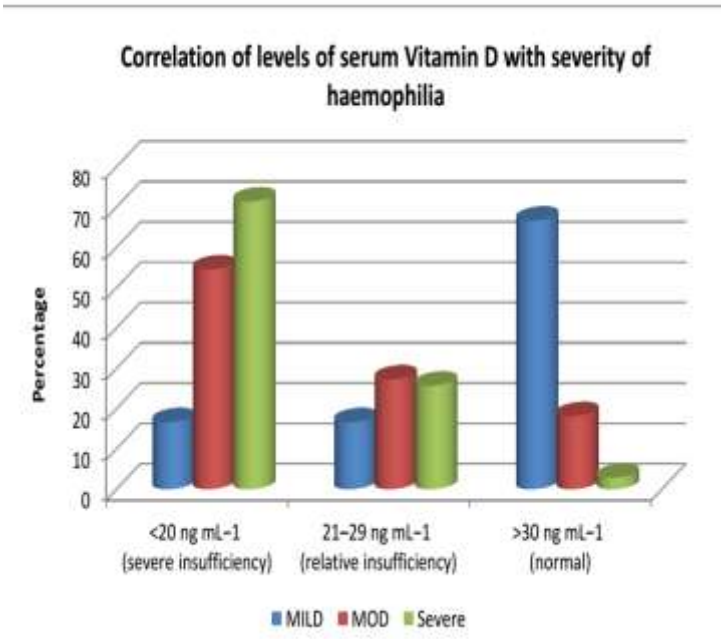
IV. Results

Association of severity of Serum Vitamin D Levels in haemophlic children with severity of the hemophilia

	MILD		**MOD**		**Severe**	
	No	%	No	%	No	%
<20 ng mL^{-1} (severe insufficiency)	2	16.67	18	54.55	25	71.43
21–29 ng mL^{-1} (relative insufficiency)	2	16.67	9	27.27	9	25.71
>30 ng mL^{-1} (normal)	8	66.67	6	18.18	1	2.86
Total	12	100.00	33	100.00	35	100.00

Chi-square = 24.617 with 4 degrees of freedom; P <0.001S

Significant association was observed for severity of Serum Vitamin D Levels in Haemophlic children with severity of the hemophilia.Lower vitamin D levels were observed as severity increases.

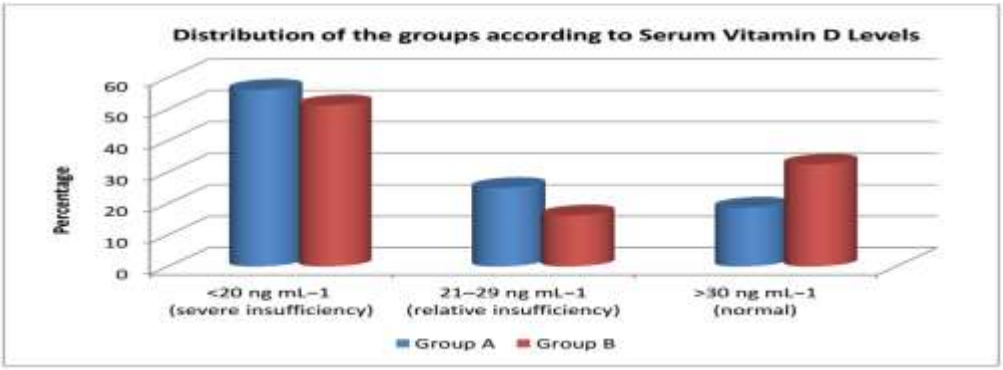


Distribution of the groups according to Serum Vitamin D Levels

	Group A		Group B		Grand Total
	No	%	No	%	
<20 ng mL^{-1} (severe insufficiency)	45	56.25	41	51.25	86
21–29 ng mL^{-1} (relative insufficiency)	20	25	13	16.25	33
>30 ng mL^{-1} (normal)	15	18.75	26	32.5	41
	80	100	80	100	160

Chi-square = 4.622 with 2 degrees of freedom; P = 0.099 NS

Although the almost 50% cases were in severe insufficiency of the vitamin D level in both the groups. relative insufficiency were more in cases as compared to control group(25%vs 16.25% but these findings were not statistically significant.



V. Disscussion

The present study is a hospital based analytic type of observational study conducted in SPMCHI, Jaipur over a period of one year. This study is one of the very few studies which aims to assess serum vitamin D levels of hemophilia patients. total 80 hemophilia patients and 80 age and sex matched control were investigated for evaluation of Serum vitamin D levels. Out of 80 hemophilia patients investigated 64(80%) were hemophilia A patients and 16 (20%) had hemophilia B. All the hemophilia patients studied were males who had received factor concentrates or blood products at least once. Almost all the patients studied had received plasma derived Factor VIII and IX concentrates. All the patients screened had been receiving episodic (on demand) therapy. None was on prophylactic factor therapy. The Hemophilia A & B patients and controls were almost equally distributed among all the age groups. Among 80 Hemophilia patients screened in our study 36 (45.00%) were having severe hemophilia A, 33 (41.25%) had moderate hemophilia and 53 11(13.75%) had mild hemophilia. The definition of severe hemophilia in the present study was kept as factor VIII or IX level <1% .

Anthropometric profile: In our study , the mean height of cases was 128.12±25.23 cms and that of the healthy controls was 126.83±25.o4 cms and the difference was statistically not significant (p>0.05). The mean weight of cases was 27.08+13.82 kgs and that of healthy controls was 29.86 +10.63 kgs and the difference was statistically not significant (p>.05). Barnes et al(2004) in their study on 19 hemophilic children found no significant difference in weight and height when compared to healthy matched controls. Similar results were found in study conducted by Abdelrazik et al. inspite of immunological abnormalities attributed to factor substitution therapy or bleeding episode in joint with potential effect on growth plate, growth in haemophilia children is not affected. Similar results are also found in study conducted by Susannas A Ranta. Serum Vitamin D levels In our study mean serum vitamin D levels in group A is 21.18(±8.49) and in group B is 21.96(±9.50) and there were no statistically significant difference is observed in mean serum vitamin D levels in cases and controls and the results are in accordance with the study conducted by Susannas A Ranta in December 2010 at university of Helsinki there mean serum vitamin D 54 in patients was 47±17 and in the controls it was 44±12 and the difference was not statistically significant[(3)]. Similar results was obtain in a study conducted by Gallacher SJ in 1994 and the explanation for the above observation is that the prevalence of vitamin d insufficiency is very high in Indian population. In our study we found statistically significant correlation between serum Vitamin D levels and severity of Haemophilia. As the severity of haemophilia increases severity of vitamin D deficiency also increases. Similar results were found in

study conducted by Linari et al in Greece. The possible explanation for the above observation is that more severe haemophilia results in more severe joint bleeds and more frequent episodes of joint bleeds which leads to prolong immobility and reduced sun exposure which leads to more severe insufficiency of vitamin D

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