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RESEARCH ARTICLE

ROLE OF VITAMIN D ON TREATMENT OF BRONCHIOLITIS IN CHILDREN

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Abstract

Background: Vitamin D plays a major role in growth and development of children. Optimal levels of vitamin D in first year of life are found to be preventive for lower respiratory tract infections.

Aim of Study: To assess the effect of vitamin D supplementation on treatment of bronchiolitis.

Patients and methods: This study is prospective follow up study conducted in Pediatric Wards of Al-Imamain Medical city in Baghdad through the period from 1st of January, 2018 to 31st of January, 2019 on convenient sample of 200 children with bronchiolitis divided into two group .group A include 98 children who were managed by traditional treatment of bronchiolitis (oxygen ,fluid ,frequent sucking of secretion) and V.D supplementation (400 iu)daily and group B that include 102 children managed with traditional treatment only . The vital signs and hospital stay duration of children were assessed daily .

Results: No significant differences were observed between two study groups regarding demographic, social, clinical and feeding characteristics. Also no significant differences were observed regarding respiratory rate at admission and at discharge. There was a significant difference regarding heart rate at discharge ($p=0.05$). A significant association was observed between children with vitamin D and shorter hospital stay duration ($p<0.001$).

Conclusions: Vitamin D supplementation is important in treatment of bronchiolitis.

Introduction:-

Vitamin D, or the "sunshine vitamin," is not just a vitamin; it is also a prohormone with numerous functions in the body. "Prohormone" refers to a group of fat-soluble secosteroids. The best-understood function of vitamin D is in the absorption of calcium from the small intestine, which helps to prevent diseases such as osteoporosis and osteomalacia in adults and rickets in children [(1)].

In addition to its important role in skeletal development and maintenance, there is increasing evidence that vitamin D has a beneficial effect on extraskeletal tissues. Tissues such as the brain, heart, stomach, pancreas, lymphatics, skin, gonads, and prostrate tissue are composed of cells, including T and B lymphocytes, that express the vitamin D receptor (VDR). In these tissues, vitamin D is thought to have roles in the improvement of immune function and the reduction of inflammation [(2)].

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Vitamin D supplementation in the first year of life has also been associated with a reduced risk of lower respiratory tract infections (LRIs) and reduced recovery time in infants with acute bronchiolitis [3].

Bronchiolitis is the most common acute lower respiratory tract infection of viral origin among infants. It is characterized by cough, rhinorrhea, crackles, wheezes, fever, and hypoxemia. Common etiology includes respiratory syncytial virus, rhinovirus, adenovirus, coronavirus, human metapneumovirus, influenza, or parainfluenza. The economic and social implications of bronchiolitis are substantial. In North America, hospitalizations attributable to bronchiolitis have increased twofold over the past two decades. The disease currently accounts for more than 100 thousand hospital admissions annually at an estimated cost of $1.73 billion. In the United Kingdom, 1 in 3 infants will develop bronchiolitis in the first year of life and 2 to 3% of all infants require hospital admissions. In England alone, there were 30,451 secondary care admissions for bronchiolitis between 2011 and 2012 [4].

The diagnosis of bronchiolitis is primarily clinical. The American Association of Pediatrics defines bronchiolitis as a set of clinical signs and symptoms, including initial viral upper respiratory manifestations followed by increased respiratory effort and wheezing in children younger than 2 years. Signs of increased respiratory effort include tachypnea, nasal flaring, and chest retractions. Current evidence does not support obtaining routine chest radiography for children with bronchiolitis [5]

A possible connection between vitamin D deficiency (VDD) and respiratory infections has been proposed. As early as 1975, Salimpour studied 200 rachitic children (rickets is caused by VDD and calcium deficiency), ages 0 to 14 years, in Tehran, Iran, and found that 43% also had pneumonia. Research also has associated VDD with acute lower respiratory tract infection (ALRI), which includes bronchiolitis and pneumonia . The association between ALRI and VDD is important because ALRI is costly and a leading cause of global child mortality, annually accounting for approximately 1.4 million deaths of children younger than 5 years [6].

Globally in 2010, there were an estimated 15 million hospitalizations of children with severe or very severe ALRI [7]. In the United States, hospitalization costs for respiratory syncytial virus (RSV) infections, a common cause of bronchiolitis, range from an average of $5069 for children without underlying comorbidity to an average of $12,103 for children with chronic lung disease. If vitamin D could prevent ALRI or decrease the duration and/or severity of ALRI in children, it could save lives and decrease health care costs [8].

Recently, the harmful effects of pathogens that cause bronchiolitis have strengthened, possibly due to increasing rates of vitamin D deficiency within infants. Vitamin D has been demonstrated to play roles in both immune system activation and the prevention of infections by microorganisms. An increased risk of respiratory system diseases has been demonstrated in the first three months in infants with low vitamin D levels in the cord blood at birth [9].

Aim of Study:
To assess the effect of vitamin D supplementation on treatment of bronchiolitis.

Patients and Methods:-

This study is prospective follow up study conducted in Pediatric Wards of Al-Imamain Al-Kadhumain Medical city in Baghdad through the period from 1st of January, 2018 to 31st of January, 2019.

All children with bronchiolitis admitted to Pediatric Wards of Al-Imamain Al-Kadhumain Medical city were included in the study and we exclude the following

1. Children younger or older than 1-24 months.
2. Possibility of Asthma.
3. Possibility of Pneumonia(either by clinical or radiological method)
4. Deteriorated health status.
5. Congenital anomalies.
6. Parents refused to participate.

A convenient sample of 200 children with bronchiolitis admitted to Pediatric Wards of Al-Imamain Al-Kadhumain Medical city was selected and they were divided into two group

Group A :
include 98 children who were received in addition to traditional treatment (oxygen , fluid , and frequent suction) vitamin D.
Group B:
included c 102 children who were treated by traditional treatment only .

The data were collected directly from the children parents. The questionnaire included the followings.
1. Demographic characteristics of children with bronchiolitis: Age and gender.
2. Social and clinical characteristics of children with bronchiolitis: Residence, family history of atopy, smoking exposure and crowded environment.
3. Vital signs of children with bronchiolitis: Heart rate at admission and discharge with respiratory rate at admission and discharge.
4. Feeding history of children with bronchiolitis.
5. Hospital stays duration of children with bronchiolitis.

After admission to the ward, the children were assessed by the researcher through full history and examination. Diagnosis of bronchiolitis was confirmed by Pediatrician in the ward according to symtoms, signs and x-ray. The children were grouped into vitamin D group and no vitamin D group. The vitamin D were supplied for the selected children daily morning by the researcher by supplementation of TeraD oral drops 400 I.U. (each 1ml of TeraD drops containing 400 IU). The vital signs were measured by the researcher daily morning from admission until discharge. The children of two groups were followed up by the researcher daily until their discharge. The age of children with bronchiolitis were categorized into three groups (1-6 months), (7-12 months) and (13-24 months).

Statistical analysis:
All children's data entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 20 was used. Descriptive statistics presented as (mean ± standard deviation) and frequencies as percentages. Multiple contingency tables conducted and appropriate statistical tests performed, Chi square test used for categorical variables (Fishers exact test was used when total of expected variables was less than 20%). Independent sample t-test was used to compare between two means. In all statistical analysis, level of significance (p value) set at ≤ 0.05.

Results:-
This study show no significant difference in age between two group (group A& B) since p=0.3. Generally, males with bronchiolitis were more than females, there was no significant difference in gender between two groups as P value =0.1. All these findings were shown in table 1.

Table 1:- Distribution of demographic characteristics of children with bronchiolitis according to vitamin D intake.

Variable	Group A		Group B		P
	No.	%	No.	%	
Age					0.3*NS
1-6 months	75	76.5	69	67.6	
7-12 months	20	20.4	30	29.4	
13-24 months	3	3.1	3	3.0	
Gender					0.1*NS
Male	81	82.7	75	73.5	
Female	17	17.3	27	26.5	

* Fishers exact test, ** Chi-square test, NS=Not significant.

Also there is no significant differences between two groups regarding residence (p=0.5), family history of atopy (p=0.5), smoking exposure (p=0.08) , crowded environment (p=0.7) and smoking exposure(0.08) as shown in table 2.

Table 2:- Distribution of social and clinical characteristics according to vitamin D intake.

Variable	Vitamin D		No vitamin D		P
	No.	%	No.	%	

Residence					0.5*^{NS}
Urban	51	52.0	59	57.8	
Rural	47	48.0	43	42.2	
Family history of atopy					0.5*^{NS}
Positive	57	58.2	64	62.7	
Negative	41	41.8	38	37.3	
Smoking exposure					0.08*^{NS}
Positive	65	66.3	79	77.5	
Negative	33	33.7	23	22.5	
Crowded environment					0.7*^{NS}
Yes	30	30.6	33	32.4	
No	68	69.4	69	67.6	

* Chi-square test, S=Significant, NS=Not significant.

Mean heart rate of children in group A t admission was 114±13 b/m, while mean heart rate of children in group B at admission was 114.6±13.5 b/m, with no significant difference between them (p=0.7). While the mean heart rate of children in group A at discharge was 108.2±9.6 b/m which was significantly lower than mean heart rate of children in other group at discharge was 111.1±11.2 b/m (p=0.05). Mean respiratory rate of children in group A was 57.9±10.9 r/m, while mean respiratory rate of children in group B at admission was 58.3±8.4 r/m, with no significant difference between them (p=0.7). Also there is no significant difference was observed in mean respiratory rate at discharge between them (p=0.1). All these findings were shown in table 3 .

Table 3:- Distribution of vital signs means according to vitamin D intake.

Vital signs	**Group A**	**Group B**	**P**
	Mean±D	**Mean±D**	
HR at admission (b/m)	114±13	114.6±13.5	0.7*^{NS}
HR at discharge (b/m)	108.2±9.6	111.1±11.2	**0.05***^{S}
RR at admission (r/m)	57.9±10.9	58.3±8.4	0.7*^{NS}
RR at discharge (r/m)	36.9±0.3	37.6±5.1	0.1*^{NS}

*Independent sample t-test, NS=Not significant, S=Significant.

The common feeding types of children in group A were bottle feeding 47 (48%), breast feeding 24 (24.5%), mixed feeding 13 (13.3%).while in group B were bottle feeding 55 (53.9%), breast feeding23 (22.6%), bottle feeding and ordinary foods 14 (13.7%) respectively which statistically not significant as p value =0.2. All these findings were shown in table 4.

Table 4:- Distribution of feeding types of children with bronchiolitis according to vitamin D intake.

Variable	**Vitamin D**		**No vitamin D**		**P**
	No.	**%**	**No.**	**%**	
Feeding types					0.2*^{NS}
Breast feeding	24	24.5	23	22.6	
Bottle feeding	47	48.0	55	53.9	
Mixed feeding	13	13.3	8	7.8	
Bottle feeding and ordinary foods	8	8.2	14	13.7	
Breast feeding and ordinary food	3	3.1	0	-	
Ordinary food	3	3.1	2	2.0	

* Fishers exact test, NS=Not significant.

Mean hospital stay duration of children in group A was 2.5 days, while mean hospital stay duration of children in group B was 4.6 days, with a highly significant difference between both groups (p<0.001). as shown in table 5 and figure 2.

Table 5:- Distribution of hospital stay duration mean according to vitamin D intake.

Vital signs	**Vitamin D**	**No vitamin D**	**P**
	Mean±D	**Mean±D**	
Hospital stay duration (days)	2.5±0.7	4.6±1.6	**<0.001***^{S}

*Independent sample t-test, S=Significant.

Discussion:-

In our study, the age of children with bronchiolitis was mainly within 1-6 months with predominance of male gender (82.7%). This finding is in agreement with results of Al-Janabi et al [10] study in Iraq which reported that majority of children with bronchiolitis were males with age of less than 6 months. The residence of bronchiolitis children in present study was commonly urban. This finding is consistent with results of Hamid et al [11] study in Bangladesh and attributed this difference to air pollution and crowding environment in urban areas. The family history of atopy was relatively high among children with bronchiolitis. Similarly, Trefny et al [12] study in Switzerland found that children with positive family history of atopy had a significantly higher risk of developing bronchiolitis in earlier periods of life. Smoking exposure of children with bronchiolitis in our study was high. Farzana et al [13] stated that increase exposure of children to parental smoking is significantly accompanied by higher risk of developing severe bronchiolitis. In our study, about one third of children with bronchiolitis were living in crowded environment.

Rida study in Iraq [14] found that living in the crowded environment is a common risk factor for development of bronchiolitis among children. Unfortunately, high proportion of children with bronchiolitis in our study was on bottle feeding. This finding coincides with results of Lanari et al [15] study in Italy which found that breast feeding even mixed with bottle feeding is preventive for bronchiolitis and decreases the hospital stay.

Present study showed that mean heart rate of children received vitamin D intake at discharge was (108.2b/m) which was significantly lower than (111.1b/m) mean heart rate of children not received vitamin D intake at discharge ($p=0.05$). This finding is consistent with results of Kua and Lee systematic review study in Malaysia [25] which reported that heart rate of infants with bronchiolitis was decreased at discharge but the other primary outcome measures were not accompanied good benefits to encourage the mandatory supplementation of vitamin D for mothers and infants as preventive for bronchiolitis in infants. On other hand, Esposito and Lelii study in Italy [1] found that vitamin D was an effective and inexpensive prophylactic measure of lower respiratory tract infections in children. Recently, a study conducted in USA stated that vitamin D supplementation for neonates had a significant role in prevention of respiratory infections and improve the respiratory rate and heart rate at discharge [16]. Inconsistently, Beigelman et al [17] study in USA found that vitamin D intake by children was not related to severity indicators (respiratory and heart rates) of respiratory bronchiolitis. Halasa et al [18] study in Jordan documented that low vitamin D is an important risk factor for high rates of bronchiolitis caused by respiratory syncytial virus among Jordanian children. In Iraq, it was found that vitamin D deficiency among children is associated with increase severity of asthma and increase the chance of lower respiratory tract infections among asthmatic children [19].

Current study revealed no significant difference in respiratory rate at discharge between children with vitamin D and those with no vitamin D. This finding is similar to Rajshekhar et al [20] study in India which found that supplementation of vitamin D to less than 5 years age children with pneumonia would not improve the primary outcomes. This finding regarding respiratory rate is inconsistent with results of Erol et al [21] study in Turkey which found that vitamin D deficiency was associated with severity of bronchiolitis in children. Many authors proved that vitamin D deficiency in both mothers and children was associated with high risk of acute lower respiratory tract infections [22], while others reported no significant association between vitamin D deficiency and acute lower respiratory tract infections [23]. Although these differences, many literatures recommended the supplementation of vitamin D to children with bronchiolitis as its supply is not accompanied by serious side effects [17].

In present study, the mean hospital stay duration for bronciolitis children with vitamin D was significantly shorter than children with no vitamin D ($p<0.001$). This finding coincides with results of many literatures such as Saad et al [24] study in Egypt, Allen et al [25] study in UK and Belderbos et al[26] study in Netherlands which all found that supplementing infants and children who had bronchiolitis with vitamin D had an obvious role in decreasing the hospitalization duration which represented a highly cost benefit characteristic.

Dotta et al [27] stated that shorter hospitalization is an important preventive measure for infants and younger age children with bronchiolitis as this shorter hospitalization would decrease the risk of hospital acquired infections in addition to cost benefits. Recent American study reported that vitamin D supplementation for mothers during pregnancy is accompanied by better outcomes in prevention of bronchiolitis and decreasing hospitalization period for infants with bronchiolitis[28].

Conclusions:-

1. The vitamin D supplementation for children with bronchiolitis is accompanied by shorter hospital stay of children.
2. The risk factors for bronchiolitis in children are younger age, male gender, urban residence, family history of atopy, smoking exposure, crowded environment and bottle feeding.

Recommendations:-

1. Emphasis on inclusion of vitamin D within treatment protocols of children with brinchiolitis.
2. Strengthening children bronchiolitis preventive programs by supplementation of vitamin D within acceptable doses.
3. More researches on role of vitamin D in prevention and treatment of childhood bronchiolitis must be supported.

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