Serum Levels of 25- hydroxy Vit D3, Paraoxonase 1 and Malondialdehyde in Infants with Acute Lower Respiratory Tract Infections: Interventional Study

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Summary

Background: Acute Lower Respiratory Tract Infections. (ALRTIs) are main cause of mortality among children and represented by pneumonia and bronchiolitis. Vitamin D (Vit.D) is a steroid hormone and has major role in bone development and immunological role via Vit.D receptors in immune cells. Paraoxonase 1 (PON1) is an antioxidant enzyme and its serum concentration is influenced by inflammatory changes. Malondialdehyde (MDA) level is sensitive indicator of lipid peroxidation and oxidative stress.

Aim: To measure serum levels of Vit.D3, PON1 and MDA and to study relation of vit.D deficiency and oxidative stress in ALRTIs in infants.

Methods: A case- control (Interventional) study was done during 2019, included 35 infants with ALRTIs and 35 healthy control. S erum Vit.D3 level was measured by ELIZA. PON 1 and MDA levels were measured by spectrometer. Cases of deficiency and insufficiency received VitD supplementation. Reassessment was done after 6 months.

Results: This study included 35 infants with ALRT and 35 healthy infants as control group. Serum Vit.D3(ng/ml) showed highly significant difference between two groups, being lower in cases (mean 11.11± 5.75), vs control (31.50±7.08). In cases (94.3%) deficient, (5.7%) insufficient& no sufficient vs in control (2.9%) deficient, (40.0%) insufficient& (57.1%) sufficient. Highly significant difference of Serum (PON 1) activity (U/l)& (MDA) levels (nmol/ml) between cases and control. Highly significant differences regarding) prolonged breast feeding, socioeconomic level, introduction of food rich in vit.D, vit.D supplement during infancy and sunlight's exposure(. Significant differences regarding (overclothing, smoking exposure) and significant relation between vitD level in cases& maternal age. After intervention by therapeutic VitD supplementation and life style advise, c ases improved as 85.7% had sufficiency& 14.3% had insufficiency. Comparison of (mean Vit.D) and number of recurrences of ALRTIs (before& after) intervention between cases showed highly significant difference.

Conclusion: Association between vitD deficiency& ALRTIs in infants. PON1 and MDA may be used as parameters in diagnosis and following-up treatment of oxidative stress in ALRTIs.

KeyWords: VitD3, PON1, MDA, ALRTIs.

مستويات ٢٥ هيدروكسي فيتامين د ٣، باراً- أوكسينيز ١ ومالون داي الدهيد بالمصل في الرضع الذين يعانون من عدوي الجهاز التنفسي السفلي: دراسة تدخليه

مقدمه: عدوي الجهاز التنفسي السفلي الحاده هي السبب الرئيسي للوفيات بين الأطفال وتتمثل بشكل رئيسي في الالتهاب الرئوي والتهاب القصيبات. فيتامين (د) هو هرمون الستيرويد وله دورا رئيسيا في نمو العظام ومناعيا عبر مستقبلات بالخلايا المناعيه باراأوكسينيز ١ هو إنزيم مضاد للأكسدة ويتأثر تركيزه في المصل بالتغيرات الالتهابية، ويتم قياس مستوى مالون داي الدهيد كمؤشر لبيروكسيد الدهون، والاجهاد التاكسدي.

الهدف: قياس مستويات مصل فيتامين (د) وباراوكسيناز ومالون دايالدهايد وعلاقه نقص فيتامين (د) والاجهاد التاكسدي في عدوي الجهاز التنفسي السفلي للرضع.

الطرق: تم اجراء دراسة الحالات والشواهد (التدخلية) خلال عام ٢٠١٩، وشملت ٣٥ رضيعا مصابا و٣٥ سليما (ظابطه). تم قياس مستوى (٢٥- هيدروكسي د) بواسطه الاليزا. وقياس مستويات باراوكسيناز ومالونداي الداهيد بواسطه مقياس الطيف. تلقت حالات نقص فيتامين د مكملات علاجيه وإعادة التقييم بعد ٦ شهور.

النتائج: شملت هذه الدراسة ٣٥ حاله عدوي الجهاز التنفسي السفلي الحاده، مصل فيتامين د أقل في الحالات وأظهرت فرقا ذا دلالة إحصائية عالية بين المجموعتين. الحالات (متوسط ١١,١١ ±٥,٧٥) الظابطه (متوسط ٣١,٥٠ ±٧,٠٨) ٩٤% من الحالات لديها نقص فيتامين (د) و٥,٧% لديه قصور. بل يوجد مستوى كاف لفيتامين (د) في الحالات، الظابطه ٢,٩% لديه نقص، ٤٠% قصور، ٥٧% كاف. هناك فروق ذات دلاله احصائيه عاليه بمستوي نشاط باروكسيناز ١ (وحده/ لتر) ومالون داي الدهايد (نانومول/ مل). وايضا بما يتعلق (بالرضاعة الطبيعية المطولة، والمستوى الاجتماعي والاقتصادي، وإدخال الأطعمة الغنية بفيتامين (د)، ومكملات فيتامين (د) أثناء الرضاعة والتعرض لأشعة الشمس). وفيما يتعلق بالملابس الزائدة والتعرض للتدخين والارتباطات بين مستوى فيتامين (د) في الحالات وعمر الأم، وجدت فروق ذات دلالة إحصائية. تحسنت حالات نقص فيتامين (د) بعد التدخل بواسطه مكملات علاجيه ونصيحه فيما يخص نمط الحياه، حيث ٨٥,٧% لديهم كفاية و١٤,٣% لديهم قصور. أظهر مقارنه متوسط فيتامين (د) وعدد مرات تكرار العدوي بين الحالات قبل وبعد التدخل فرقا ذا دلالة إحصائية عاليه.

الخلاصه: ارتباط نقص فيتامين (د) وعدوي الجهاز التنفسي السفلي في الرضع. الباراوكسينيز والمالون داي الدهايد يمكن استخدامها كمعلمات لتشخيص ومتابعة علاج الإجهاد التأكسدي.

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Introduction:

Acute lower respiratory infections (ALRTIs) are the main cause of morbidity and mortality among children and are mainly represented by community- acquired pneumonia (CAP) and acute bronchiolitis. (De Souzaa, et.al, 2018)

Thirty child deaths are attributed to CAP in developing countries, with two- thirds of these deaths occurring during infancy. (Li, et.al, 2018)

Vitamin D (Vit.D) is a steroid hormone and plays a major role in bone development. Circulating 25(OH)vit.D3 concentrations provide a useful index of vit.D status that reflects dietary intake and sunshine exposure (Gharehbaghi, et.al, 2018). In the pediatric population, it is associated with life style manners, such as clothing, high latitudes, low consumption, and little sun exposure. (Cediel, et.al, 2018)

Vit.D3 deficiency (VDD) is defined as a serum [25(OH) D3] level equal to or less than 20 ng/mL, whereas vitamin (D3) insufficiency is defined as a serum level between 21 and 29 ng/ mL. A sufficient Vitamin (D) level is accepted as >30 ng/mL (75 nmol/L). (Erol al, 2017)

There are reports that suggest vital and complex role of Vitamin (D) in immune system function and regulation (Gharehbaghi, et.al, 2018). Reports are inconsistent on the role of vit.D in lower respiratory tract infections. (Mahyar, et.al, 2017)

The action of Vitamin (D) is mediated via vit.D receptors, which are in all types of immune cells. Vit.D deficiency affects immune function to decrease the host defenses against infections in children (Li, et.al, 2018). Also vit.D maybe a potent antioxidative. (Igde, et.al, 2018)

The imbalance between oxidant and the antioxidant causes oxidative stress which is considered to play an important role in the pathogenesis of lung diseases (Dag, et.al, 2018). Antioxidant tests have moved from the research into routine Clinical Chemistry, and now part of general health screening programs. (Akunueze, et.al, 2018)

Paraoxonase 1 (PON1) is a glycoprotein. It is an antioxidant enzyme& Its serum concentration is influenced by inflammatory changes (Vaidya& Bulakh, 2013). Malondialdehyde (MDA) level is used as one of the most sensitive indicators of lipid peroxidation, and hence oxidative stress. (Dag, et.al, 2018). Antioxidant tests have moved from the research into routine Clinical Chemistry, and now part of general health screening programs. (Akunueze, et.al, 2018)

Aim Of The Study:

This study aimed to measure serum levels of (25(OH)Vit.D3), paraoxonase1 and malondialdehyde to determine incidence and relation of vit.D deficiency (VDD) and oxidative stress in ALRTIs in infants.

Subjects And Methods:

A case- control (Interventional) study was done, included 35 infants with ALRTIs (case group) and 35 healthy infants of the same age (control group). It was conducted in outpatient Clinic of Pediatrics of El Tahrir general hospital, in North Giza Governorate, during the year of 2019:

- Inclusion criteria: The age of the infants ranged between (2- 24) months. cases were diagnosed as acute bronchiolitis& pneumonia. Exclusion criteria: Children with comorbidities and underlying chronic conditions. Detailed full history taking, Clinical examination and radiological investigations were conducted.
- Laboratory investigations: A 5ml of venous blood samples were collected under sterile conditions from cases& control subject& centrifuged to separate serum samples which were stored at −15°C, then were analyzed for measurement of the following parameters:
  1. Serum 25(OH)vit.D level: It was measured by enzyme liked immunosorbent assay (ELIZA) technique (Heureux, et.al, 2015). The 25 OH vitamin D Enzyme Immunoassay (EIA) kit (KT- 715) was used for the quantitative measurement of total 25(OH)vit.D in serum and plasma. It was manufactured at Epitope immune Diagnostics (EDI), Inc in USA. Serum 25(OH)vit.D level was expressed in (ng/ ml).
  2. Serum paraoxonase (PON1) level: Arylesterase activity of paraoxonase was measured in serum by Spectrophotometer (Cioabla, 2013) using phenylacetate as substrate. The cleavage of phenyl acetate resulting in phenol (Watson, et.al., 1995). The activity was expressed in U/L (U is the abbreviation of unit of enzyme activity, and is defined as the amount of enzyme that catalyzes the conversion of 1micro mole of substrate per minute).
  3. Serum Malondialdehyde (MDA) level: It was measured by Spectrophotometer (Cioabla, 2013). It was determined in serum samples according to the method described by Ruiz- Larrea, et.al. (1994). Thiobarbituric acid (TBA) was reacted with Malondialdehyde in acidic mediumate temperature 95°C for 30 min to form Thiobarbituric acid reactive product, the resultant pink product was measured at 534nm. The kit was supplied from Bio- diagnostic Company. The MDA level was expressed in (nmol/ml).
- Intervention: Cases of vit.D3 deficiency or insufficiency received Life style advise (proper sun exposure and adequate intake food rich with vit.D3& with Calcium). Also Vit.D3 (therapeutic dose 1000- 2000IU/ day for six months) (Lee, et.al, 2013), (Folsom& DiMeglio, 2017)& (Cediel, et.al, 2018). Supplementation was prescribed in form of syrup (5ml once or twice daily). Each 5ml contain (1000 IU vit.D3+ 6.5 mg Calcium+ 10 mcg vit B12). After 6 months of supplementation, Serum level of Vit.D3 was reassessed and also history of recurrence of ALRTI during this period.
- Ethical Considerations:
  1. For each case, a written consent was signed personally by one of the parents after explanation of the aim of the study& the importance of detection of vit.D deficiency, its possible effect on immunity, possible relation to respiratory infections and the importance of treatment of this deficiency.
  2. This study and method were agreed upon by Human Ethical Committee of Medical Studies Department, Faculty of Postgraduate Childhood Studies, Ain Shams University, then

following the instructions of HELSINKI.

3. Privacy and confidentiality: All data and information were taken from the patients had a high degree of confidentiality. Samples for laboratory investigations were discarded and would not be used in other researches.

Statistical Analysis:

The collected data were tabulated, graphically presented and statistically analyzed in terms of range, mean, standard deviation (SD), median, frequencies. A probability value (P-value) less than 0.05 will be considered significant. All statistical calculation was done by using computer programs Microsoft Excel 2012 and SPSS version12. (Mostafa& El Shourbagy, 2012)

Results:

This study included 70 infants: 35 cases and 35 control. 35 cases of ALRTIs, 18 infants were diagnosed as bronchiolitis (51.4%)& 17 infants (48.6%) were diagnosed as pneumonia. 54.3% (n= 19) cases were males and (45.7%) (n= 16) were females. Age (months) mean± SD 11.0± 7.2, median 9.0& range: (2- 24). weight (kg) mean± SD was 8.4± 2.6, median 8& range: (4- 16). 48.6% (n= 17) of cases were rural, 51.4% (n= 18) were urban.

Table (1) Comparison between cases and control as regards laboratory measurements (before intervention) (Mean, SD, Range& P-value)

Variable		Mean	SD	Range	P Value
Serum 25(OH)Vit.D3 level (ng/ml) before intervention	Cases	11.1054	5.75334	2.95- 25.53	<0.001**
	Controls	31.5066	7.08224	20.09- 4 8.86	
Serum Paroxnase1(PON 1) activity level (U/l)	Cases	146.54517	42.898124	79.550- 220.610	<0.001**
	Controls	282.39266	104.264979	156.102- 5 40.340	
Malondialdehyde (MDA) level (nmol/ml)	Cases	2.66489	0.911490	1.374- 4.640	<0.001**
	Controls	1.46063	0.483355	0.840- 2.350	

Independent sample T- test.**p<0.001= highly significant differences

Table (2) Comparison in cases (before& after intervention) as regards serum Vit.D3 level

Variable	Mean	N	SD	Range	P Value
(Before intervention) serum 25(OH)Vit.D3 level (ng/ml)	11.1054	35	5.75334	2.95- 25.53	u<0.001*
(After intervention) serum 25(OH)Vit.D3 level (ng/ml)	33.037	35	4.1185	25.0- 45.0	

*Highly significant difference (p<0.001)

Table (3) Comparison Of Vitd Level In Cases& (Alrtis) Recurrences After Intervention

Variable		N	Mean	SD	Range	P Value
Number of recurrences of (ALRTIs) after intervention	Deficiency	33	0.39	0.659	0- 2	0.410
	Insufficiency	2	0.00	0.000	0- 0	

Paired sample T- test

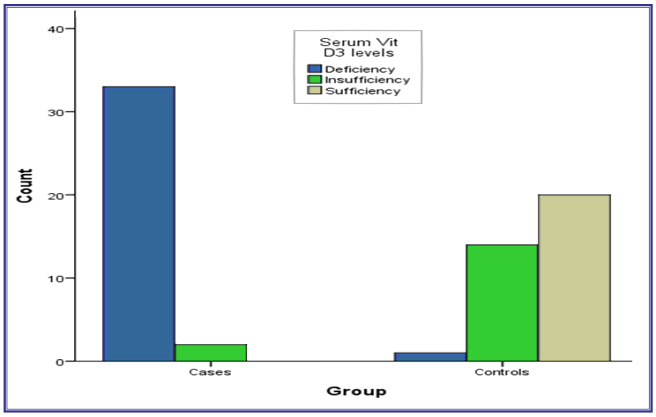

Fig (1) Highly significant difference (p< 0.001) between cases and control as regards Serum 25(OH)Vit.D3 level (ng/ml)(before intervention)

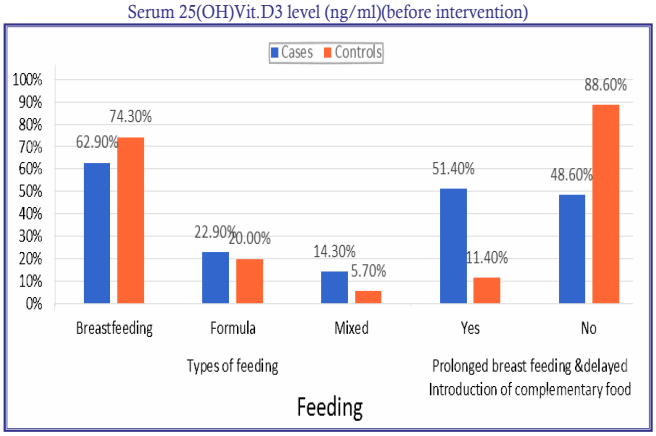

Fig (2) Comparison between cases& control. Highly significant differences (p< 0.001) as regards prolonged breast feeding& delayed Introduction of complementary food, but insignificant difference as regards type of feeding

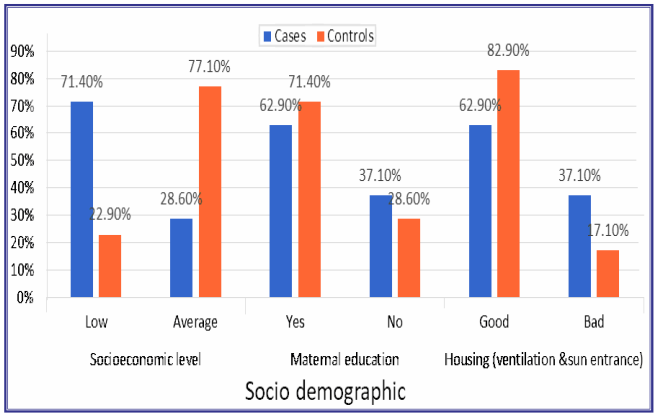

Fig (3) Comparison between cases and controls as regards socioeconomic status. Highly significant differences (p< 0.001) as regards socioeconomic level, but insignificant difference as regards maternal education& housing (ventilation& sun entrance)

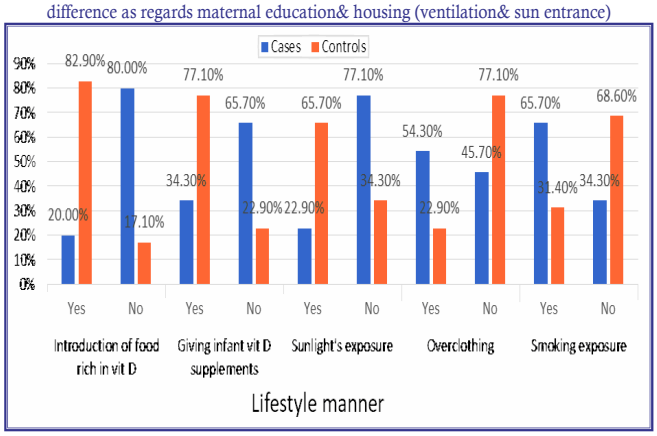

Fig (4) Comparison between cases and control. Highly significant differences (p< 0.001) as regards introduction of food rich in vit.D, vit.D supplement during infancy& sunlight's exposure. Significant differences (p< 0.05) as regards overclothing& smoking exposure

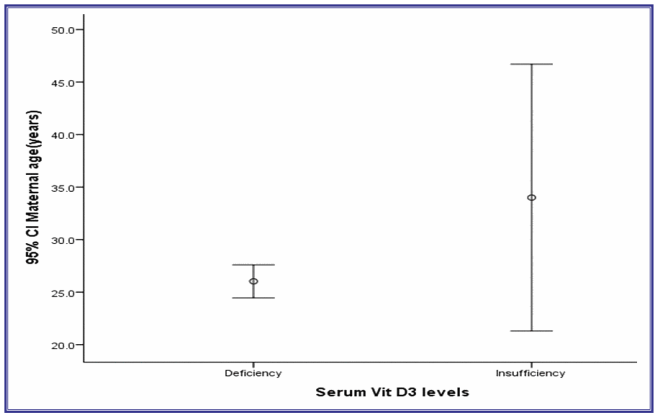

Fig (5) Comparison between vit.D level in cases& maternal age showed significant differences (p= 0.017)

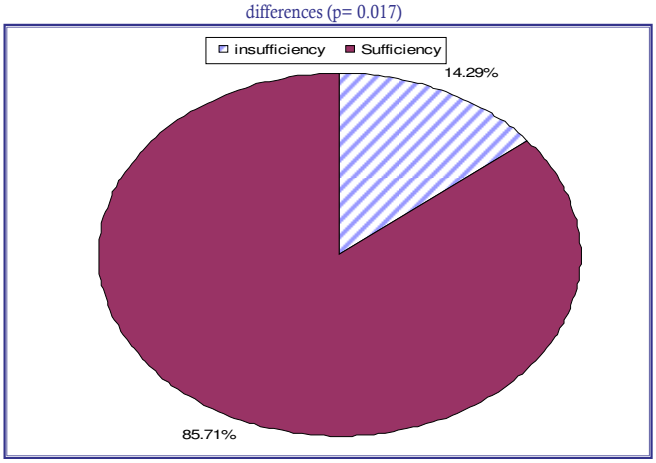

Fig (6) Reassessment of vitD3 level for cases (after intervention)

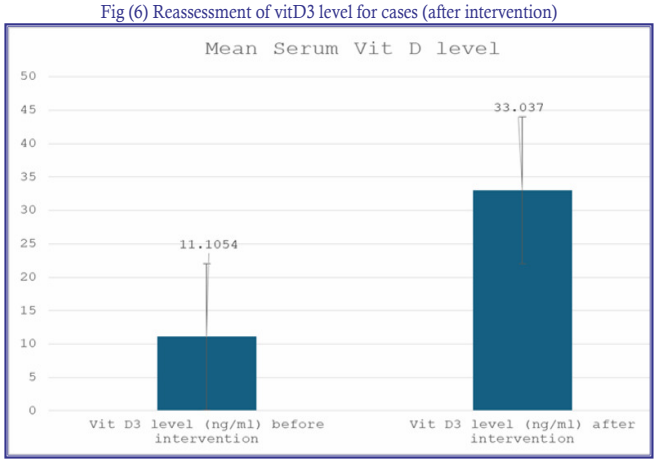

Fig (7) Comparison of the mean of vit.D before& after intervention among cases. Highly significant difference (P< 0.001)

Discussion:

In this study, serum 25(OH)Vit.D3 level (ng/ ml) was classified as: (deficiency≤ 20 ng/ml), (insufficiency 21- 29 ng/ml)& (sufficiency> 30ng/ ml) 94.3% (n= 33) of cases had deficiency, 5.7% (n= 2) had insufficiency& no sufficient vit.D level detected in cases, while 2.9% (n= 2) of control had deficiency, 40.0% (n= 14) had insufficiency& 57.1% (n= 20) had sufficient vit.D. There was highly significant difference (p <0.001) between the two groups as deficiency being higher in cases group, while insufficiency& sufficiency being lower in cases group as showed in fig (1).

Additional classification of deficiency of serum 25(OH)Vit.D3 was: very severe (<5ng/ml), sever (5- 10) ng/ ml& vit.D deficiency (10- 20) ng/ ml. 18.2% (n= 6) of cases had very severe deficiency, 27.3% (n= 9) had sever deficiency, 54.5% (n= 18) had deficiency, while no control had very severe deficiency or sever deficiency& 100.0% (n= 19) of control had deficiency. There were insignificant difference (p= 0.666) between two groups.

In current study a comparison between cases and control as regards serum 25(OH)Vit.D3 levels (ng/ ml) as showed in table (1), in cases group mean± SD of Vit.D3 levels (ng/ ml) was 11.11± 5.75& range: 2.9 5- 25.53. In control group mean± SD of Vit.D3 was 31.5066± 7.08224& range: 20.09- 48.86. There was highly significant difference (p< 0.001) between the two groups, the mean of serum Vit.D3 levels being lower in cases group.

In this study, infants with acute lower respiratory infections (ALRTIs) (bronchiolitis& pneumonia) displayed highly significantly lower Vitamin (D) levels than control group.

In agreement with current study, Golan- Tripto, et.al (2021) found that children with acute bronchiolitis displayed significantly lower Vitamin (D) levels than children with non- respiratory acute febrile illnesses. Serum 25(OH) vitamin D levels were lower in the bronchiolitis group; median 28 [18- 52] nmol/ L and 50 [25- 79] nmol/ L, respectively, p> 0.005. Deficient 25(OH) Vitamin (D) levels (< 50 nmol/L) were found more frequently in the bronchiolitis group than in the control group and sufficient 25(OH) vitamin D levels were found more frequently in the control group than in the bronchiolitis group. Also Oktaria, et.al (2021) found that Vitamin (D) deficiency was common in under- five children hospitalized with pneumonia, but was not related to pneumonia severity and hospitalization outcomes.

In this study as regards infant age, there was no significant difference (p= 0.157) as a comparison between cases and control. The mean± SD infant age for cases was 11.000 months± 7.2396& range: 2.0- 24.0 vs mean± SD was 13.243 months± 5.7782& range: 2.0- 24.0 in control group.

In contrary to current results, Oktaria, et.al (2021) found that young age (<6 months) was risk factors for severe pneumonia. Also, Al- Qahtani, et.al (2022) found the mean serum level of Vitamin (D) was significantly low among infants compared to children aged 12 months& more.

On the other hand, the study by Li W, et.al (2018) examined vit.D level in children aged (3 days to 14 years)& found that the serum 25(OH)D levels differed in children of different ages. With increasing age, serum 25(OH)D concentration gradually decreased, with the highest values observed from zero to 11 months group and lowest in the 84- months group.

In the current study as regards infant sex, there were no significant difference (P= 0.467) as a comparison between cases and controls In cases group, 19 patients out of 35 (54.3%) were males and 16 patients (45.7%) were females. As regards control, 22 healthy infants out of 35 (62.9% %) were male and 13 (37.1%) were females. The current results were consistent with a study by Wei Li, et.al (2018) that found there were no significant differences between the boys& girls.

In contrary to current results, Al- Qahtani, et.al (2022) observed that males, infants, had a significantly lower level of mean serum vitamin

levels and a higher prevalence of Vitamin (D) deficiency. The findings of males having lower levels of Vitamin (D) and a higher rate of Vitamin (D) deficiency are different from other studies in the middle east that report a higher prevalence among females. This variation may be due to differences in the study population and different settings, such as in this research, which investigated infants, whereas the other studies analyzed adolescents and adult females. Another reason for these differences may be the study setting, which was hospital- based in our case, rather than in the community

In current study, in comparison between cases& control the weight of cases ranged between (4- 16) kg with mean± SD 8.429± 2.5786& the weight of control ranged between 5.5- 12 with mean± SD 9.443± 1.8581. There was insignificant difference between the two groups (P= 0.063). In contrary to this results, Oktaria, et.al (2021) found that low birth weight and poor nutritional status on admission were risk factors for severe pneumonia

As regards residence, in this study there was no significant difference between two groups (P= 0.229) In cases group 48.6% (n= 17) were rural, 51.4% (n= 18) were urban vs in control group 62.9% (n= 22) rural& 37.1% (n= 13) urban.

As disagreement with current results, AL- Qahtani, et.al (2022) observed that urban dwellers had lower levels of mean serum Vitamin (D) as compared to rural dwellers. A similar urban- rural difference was observed in studies by Jayashri, et.al (2020)& Griffin, et.al (2019) in India and Malaysia. Urban living and sunlight exposure are related. In urban areas, there is a lack of space and overcrowded tenements that prevent direct sunlight from reaching inside most parts of urban regions and gives limited scope for outdoor activities among children.

Today, most children tend to spend more time indoors than outdoors. Excessive time spent indoors reduces sun exposure and, therefore, leads to decreased Vitamin (D) synthesis. Air pollution has contributed to reduce the number of solar UVB rays reaching the ground, hampering Vitamin (D) synthesis (Surve, et.al, 2017) (He, et.al, 2020). The extreme discomfort of the middle- eastern sun also keeps children away from the sunlight. This issue particularly holds true for infants, who are primarily at home and neither receive sufficient exposure through school nor during play outdoors.

In the current study, there was insignificant difference (p= 0.430) between cases& control as regards type of feeding. In cases group (62.90%) were breast- fed, (22.90%) were formula fed& (14.30%) were mixed. In Control (74.30%) were breast- fed, (20%) were formula fed& (5.70%) were mixed.

On the other hand, in current study highly significant difference (p< 0.001) between cases and controls was present as regards prolonged breast feeding& delayed Introduction of complementary food, being higher in cases group. (51.40%) of cases were prolongelly breast feed& delayed introduction of complementary food, while (48.60%) were not vs (11.40%) of control were prolongelly breast- fed, while (88.60%) were not. as showed in fig (2).

The current sample found highly significant difference (p< 0.001) as regards socioeconomic level between cases and control. low level was (71.40%) in cases vs (22.90%) in control, being higher in cases group. On the other hand, no significance difference as regards maternal education (p= 0.445)& housing (sun entrance& ventilation) (p= 0.060) between the two groups as showed in fig (3).

This was in agreement with the study by Kuti, et.al (2020) who found that the fact that 25.0% of the Nigerian children with pneumonia had Vitamin (D) deficiency (VDD) despite the abundance of sunshine all year. expectantly should have low prevalence of VDD in children; however, social practices such as prolonged breastfeeding and poor intake of Vitamin (D) rich complementary diet may contribute to increased prevalence of hypovitaminosis D observed in that study and others from similar areas with abundant sunshine. This also explains why low socio-economic class was a predictor of suboptimal Vitamin (D) in sample population. Children from low social class are often given suboptimal complimentary diets poor in dairy products that are good sources of Vitamin (D). Unfortunately, breast milk is poor in Vitamin (D) with average amount of 22 U/l (range 15- 50 U/l) in a Vitamin (D) sufficient mother.

In this study as regards life style manner as showed in fig (4), there were highly significant differences (p< 0.001) between cases and control as regards introduction of food rich in vit.D, vit.D supplements during infancy& sunlight's exposure, being higher in control group. There were significant differences as regards overclothing (p= 0.007)& smoking exposure (p= 0.004)& regards regularly or irregular vit.D supplements during infancy (p= 0.018), being higher in cases group.

Also in current study as showed in table (1), there was highly significant difference between cases and control (p<0.001) as regards serum Paroxnase1 (PON 1) activity level (U/ l), serum (PON 1) activity level (U/l), being lower in cases group. The mean± SD was 146.54517± 42.898124& range: 79.550- 220.610 in cases, while in control the mean was 282.39266± 104.264979& range:1 56.102- 540.340.

Furthermore, in this study, there was highly significant difference between cases and control (p< 0.001) as regards serum Malondialdehyde (MDA) level (nmol/ ml), being higher in cases group. The mean± SD was 2.66489± 0.911490& range: 1.374- 4.640, while in control the mean± SD was 1.46063± 0.483355 range: 0.840- 2.350. There was highly significant differences (P< 0.001) between the two groups, being higher in cases group.

These findings were in agreement with a study by Kuti, et.al (2020) found that children with community acquired pneumonia (CAP) had lower serum Vitamin (D) and antioxidants than control, and severe pneumonia was significantly associated with suboptimal serum Vitamin (D) and recommended that Vitamin (D) and antioxidant supplementation may be helpful in reducing the burden CAP in children.

In this study as regards correlations of vit.D levels& different variables

in deficiency& insufficiency group of cases (number, mean, standard deviation, range& P-value). There were insignificant difference between deficiency groups and insufficiency groups among cases as regards infant age (p= 0.373), weight (p= 0.283), age of introduction of complementary food(months)(p= 0.143), duration of symptoms (days) (p= 0.397), Serum (PON 1) activity level (U/l) (p= 0.320), (MDA) level (nmol/ ml) (p= 0.971) and number of recurrences of ALRTI during the last 6 months of follow- up period (p= 0.410)

On the other hand, Comparison between deficiency& insufficiency group among cases as regards relation of vit.D to maternal age (years) showed significant difference (p= 0.017) as showed in fig (5). The maternal age for deficiency group of cases ranged between (19- 35) years with mean± SD 26.030± 4.4264 vs the maternal age for insufficiency group of cases ranged between (33- 35) years with mean± SD 34.000± 1.4142, being lower in deficiency group than insufficiency group.

In this study, cases of vit.D3 deficiency or insufficiency received life style advise (proper sun exposure and adequate intake food rich with vit.D3& with calcium), also cases received Vit.D3 supplementation (therapeutic dose (1000- 2000) IU/ day for six months). Reassessment of serum Vit.D3 level after 6 months of intervention and follow up showed that cases improved as 85.7% (n= 30) had sufficiency& 14.3% (n= 5) had insufficiency as showed in fig (6).

In current study, as regards comparison of serum 25(OH)Vit.D3 level between cases (before& after intervention). Before intervention in cases group the mean± SD of Vit.D3 levels (ng/ml) was 11.11± 5.75, while reassessment of serum 25(OH)Vit.D3 level (ng/ml) (after 6 months intervention), the mean± SD was 33.0± 4.1. There was highly significant difference (p< 0.001) between cases (before & after intervention), being higher after intervention as showed in table (2) and fig (7).

On the other hand, in this study as showed in table (3) there was insignificant difference (p= 0.410) as regards comparison of vit.D level in cases& number of recurrences of (ALRTIs) during and after the intervention and follow- up period. In deficiency group of cases (n= 33), mean± SD was 39± 0.659& range (0- 2), while in insufficiency group of cases (n= 2), mean± SD was 0.00± 0.000& range: (0- 0)

As disagreement with current study, Hong M, et.al (2022) found a significant inverse dose- response association between vit.D intake from supplementation and the risk of developing ALRTIs throughout infancy. This finding provides preliminary evidence that the vit.D supplementation may be a possible strategy to prevent ALRTIs, and the optimal supplementation dose may be beyond the current recommendation, which is worth confirming further.

Additional studies are needed to address the diagnostic and therapeutic implications of the role of Vitamin (D) in respiratory morbidity, particularly in acute bronchiolitis& pneumonia. Future studies should be conducted to include a large number of patients that might better represent the general population.

Limitations:

Small size sample, cost of laboratory investigations& refusal of some parents to allow their children to participate.

Conclusion:

In this study, we found a highly significant difference in vit.D level between cases& control. We found an association between 25(OH) Vitamin (D) deficiency and ALRTIs. This finding suggested that inadequate Vitamin (D) status might serve as a risk factor for ALRTI& also might has beneficial important role in treatment of ALRTIs. Further more, there were highly significant difference as regard socioeconomic level& life style manner. Also, there were highly significant difference. between cases and controls (p< 0.001) as regard Serum Paroxnase1 (PON 1) activity level (U/ l)& Malondialdehyde (MDA) level (nmol/ml). values may be used as parameters in the diagnosis and following- up treatment of oxidative stress in the children with acute lower respiratory infections.

Recommendations:

Importance of providing prophylactic vit.D to Egyptian infants and consider the necessary measures to prevent vit. D3 deficiency. Vit.D3 screening to children with ALRTIs. The Vit.D supplementation may be a possible strategy for prevention or adjuvant therapy in ALRTIs. Serum (PON 1) and (MDA) values may be used as parameters in the diagnosis and following- up treatment of oxidative stress in the children with ALRTIs. Future studies should be conducted to include a large number of patients that might better represent the general population.

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