

# The Relation Between Vitamin D Level with Acute Otitis Media and its Recurrence in Children, Aden, Yemen

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## ABSTRACT

**Background:** Acute otitis media are most common pediatric diseases. Lack of vitamin D is a risk of otitis media and its recurrences.

**Objective:** To investigate the relation between vitamin D level and otitis media and its recurrences.

**Materials and method:** This retrospective study conducted in Aden, between January 2019 and December 2020.

**Results:** Eighty-five children with otitis media were studied and they were (51.8%) males and (48.2%) females. The mean age of patients was  $5.6 \pm 2.8$  years. Most of the patients (56.5%) were between 1 to 5 years old.

Fever represented (56.5%) in the age group 1 – 5 years old. The difference between values is statistically significance ( $p = 0.000$ ).

In the age group 1-5 years we found congested hyperemic tympanic membrane (43.5%) followed by the bulge tympanic membrane (9.4%).

Highly significant differences found between otoscopic findings and the age groups ( $p = 0.000$ ).

Recurrent attack of acute otitis media seems to be higher in the age group 1-5 years old; ( $p = 0.041$ ).

Most (82.3%) of the patients had deficient vitamin D level followed by patients with insufficient vitamin D level (11.8%).

The recurrent attacks in the deficient group represented with 3 times (30.5%) followed by 4 times (22.4%). Highly significant differences were found between recurrent attacks and level of vitamin D ( $p = 0.000$ ).

**Conclusion:** Our study showed relation between abnormal level of vitamin D and recurrent acute

otitis media mostly in the age group from 1-5 years.

**Key words:** Relation, vitamin D, otitis media, children.

## INTRODUCTION

Otitis media (OM) is an inflammatory condition characterized by the accumulation of fluid or effusion in the middle ear space. In OM with effusion (OME), this middle ear effusion is present without signs or symptoms of acute infection. OME may persist as chronic OM with effusion (COME) if the fluid remains for 3 months or longer. In acute OM (AOM), acute infection accompanies the effusion. <sup>[1,2]</sup> AOM may reoccur as recurrent acute OM (RAOM). Recurrent acute otitis media: either 3 or more episodes of acute otitis media occurring within a 6-month period, or at least 4–6 episodes within a 12-month period (no consensus has been reached on the latter). <sup>[1]</sup>

Recent studies related to serum 25-hydroxy vitamin D (25[OH] VD) showed that vitamin D might play a strong immunomodulatory role in improving the incidence and severity of bacterial and viral infections. <sup>[3]</sup> In addition, several studies suggested that children with low serum 25(OH) VD levels suffer from respiratory infectious diseases at a high risk. <sup>[4-9]</sup> Theoretically, the lack of vitamin D could cause an increased risk of rAOM, and vitamin D supplementation could be related

to the limitation of the number of new episodes in OM-prone children.

Vitamin D is believed to have a major role in the improvement of immune function and reduction of inflammation. Its active metabolite 1,25(OH)<sub>2</sub>D (calcitriol) has been documented to mediate in the innate and adaptive immune systems and triggers effective antimicrobial pathways against bacterial, viral, and fungal pathogens in the cells of the innate immune system. [10]

### Objective

To investigate the relation between vitamin D level and otitis media with its recurrences among children, in Aden.

### MATERIALS AND METHOD

This retrospective study was conducted at the ENT Private clinic in Aden, Yemen. The study group comprised children who were diagnosed with acute otitis media between January 2019 and December 2020. With exclusion of high risk children (Craniofacial anomalies, Rickets and Chronic medical diseases). The blood sample was taken after diagnosis of acute otitis media immediately in the laboratory for measuring of serum 25 hydroxy vit D.

The collected data were sex, age, symptoms, otoscopic findings, recurrent attacks, and serum vitamin D levels. We grouped the

levels of serum vitamin D according to grouping reported by Cayir et al. [11] They were:

Group 1: Levels < 20 ng/ml considered as vitamin D deficient.

Group 2: Level between 20 and 32 ng/ml considered as vitamin D insufficient.

Group 3: Levels between 32 and 100 ng/ml considered as adequate.

The collected data were tabulated and statistical analysis was done by estimating rates, means and standard deviations, Fisher test was used and p-value < 0.05 was considered as statistically significant. The statistical software package SPSS version 22 was used.

### RESULTS

Eighty-five children with otitis media were studied and they were 44 males (51.8%) and 41 females (48.2%), (male:female ratio 1.1 : 1). The age of patients ranged between 1 to 15 years and the mean age of all patients was 5.6 ± 2.8 years. The mean age of males was 6.2 ± 3.3 years and the mean age of females was 4.9 ± 2.1 years. There was significant difference between mean ages and sex (p < 0.05).

We noted that most of the patients were between the age 1 to 5 years 48 (56.5%). Values of variables illustrated in Table 1 and Figure 1.

**Table 1: Distribution of demographic characteristics of the patients (n = 85)**

Variable	Range	Mean	No	%	p-value
Sex:					
Females			41	48.2	
Males			44	51.8	
Male to female ratio:			1.1: 1		
Age range (years):	1 - 15				
Mean age ± SD <sup>*</sup> (years):					
All patients		5.6 ± 2.8			P < 0.05
Male patients		6.2 ± 3.3			
Female patients		4.9 ± 2.1			
Age groups (years):					
1 - 5			48	56.5	
6 - 10			31	36.5	
11 - 15			6	7.1	

SD<sup>\*</sup>: Standard deviation;

Figure 1: Distribution of study patients related to sex

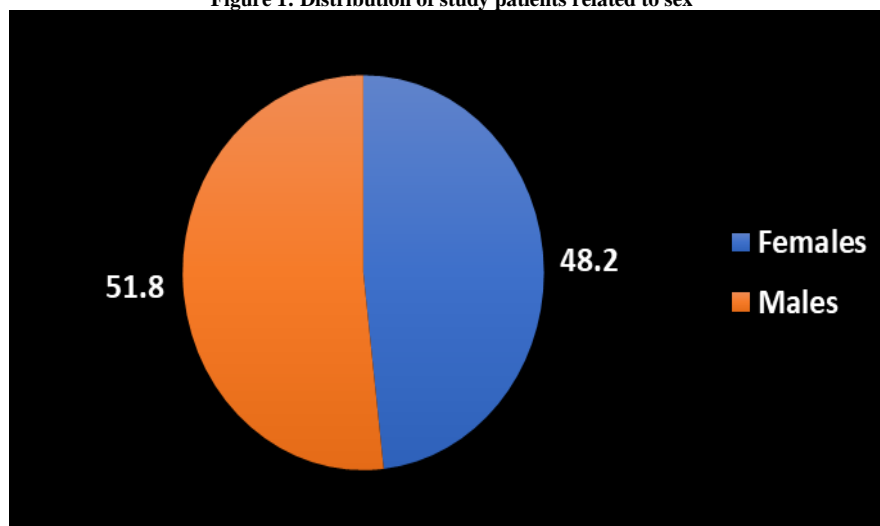


Table 2 showed the distribution of symptoms and other variables related to age groups of the study patients. Fever represented with 48 (56.5%) in the age group 1 – 5 years old followed by the age group 6 – 10 years old with 28 (32.9%). The difference between values is statistically significance ( $p = 0.000$ ). Ear pain was among all age groups. It was predominant in the age group 6 – 10 years with 31 (36.5%) followed by patients of age group 1 – 5 years with 27 (31.8%), ( $p < 0.05$ ). Upper respiratory tract infection (URTI) in the age group 6 – 10 years old was higher than in other age groups with 26 (30.6%). Irritability and crying found among patients age group 1 – 5 years with 22 (25.9%), and similar to this finding was the variable of gastrointestinal tract troubles (GIT troubles), ( $p$ -value  $< 0.05$ ).

Otoscopic findings were bulge tympanic membrane, congested hyperemic tympanic membrane and perforation with discharge. In the age group 1-5 years old we found congested hyperemic tympanic membrane

37 (43.5%) followed by the bulge tympanic membrane with 8 (9.4%) and perforation with discharge 3 (3.5%). In the age group 6 – 10 years old, the bulge tympanic membrane was the predominant with 16 (18.8%) followed by perforation with discharge 9 (10.6%). In addition, in the age group 11 – 15 years old the bulge tympanic membrane was predominant with 5 (5.9%). Highly significant differences were found between otoscopic findings and the age groups ( $p = 0.000$ ).

Recurrent attack of acute otitis media seems to be higher in the age group 1-5 years old than that in the age group 6-10 years old and the age group 11-15 years old. Significant differences were found between recurrent attacks and the age groups ( $p = 0.041$ ). The levels of serum vitamin D (deficit and insufficient, normal), seem to be higher in the age group 1 – 5 years old than in the other age groups. No significant differences were found between levels of vitamin D and the age groups ( $p > 0.05$ ).

Table 2: Distribution of symptoms, otoscopic findings and other variables related to age groups of the study patients (n=85)

Variables	Age group (years)			Total No (%)	P-value
	1 - 5 No (%)	6 - 10 No (%)	11 - 15 No (%)		
<i>Fever:</i>					
Yes	48 (56.5)	28 (32.9)	0 (0.0)	76 (89.4)	P = 0.000
No	0 (0.0)	3 (3.6)	6 (7.1)	9 (10.6)	
<i>Ear pain:</i>					
Yes	27 (31.8)	31 (36.5)	6 (7.1)	64 (75.3)	P = 0.000
No	21 (24.7)	0 (0.0)	0 (0.0)	21 (24.7)	
<i>URTI:</i>					
Yes	23 (27.1)	26 (30.6)	4 (4.7)	53 (62.4)	P = 0.003
No	25 (29.4)	5 (5.9)	2 (2.4)	32 (37.6)	

<i>Irritability and crying:</i>					
Yes	22 (25.9)	0 (0.0)	0 (0.0)	22 (25.9)	P = 0.000
No	26 (30.6)	31 (36.5)	6 (7.1)	63 (74.1)	
<i>GIT troubles:</i>					
Yes	22 (25.9)	0 (0.0)	0 (0.0)	22 (25.9)	P = 0.000
No	26 (30.6)	31 (36.5)	6 (7.1)	63 (74.1)	
<i>Otoscopy findings:</i>					
Congested HTM	37 (43.5)	6 (7.1)	0 (0.0)	43 (50.6)	P = 0.000
Bulge TM	8 (9.4)	16 (18.8)	5 (5.8)	29 (34.1)	
Perf with discharge	3 (3.5)	9 (10.6)	1 (1.2)	13 (15.3)	
<i>Recurrent attacks:</i>					
None	2 (2.4)	0 (0.0)	0 (0.0)	2 (2.4)	P = 0.041
Once	6 (7.1)	4 (4.7)	0 (0.0)	10 (11.8)	
Twice	10 (11.8)	5 (5.9)	3 (3.5)	18 (21.2)	
Three	15 (17.6)	10 (11.8)	1 (1.2)	26 (30.6)	
Four	9 (10.6)	10 (11.8)	0 (0.0)	19 (22.4)	
Five	6 (7.1)	2 (2.4)	2 (2.4)	10 (11.8)	
<i>Level of vitamin D:</i>					
Deficit	39 (45.8)	27 (31.8)	4 (4.7)	70 (82.3)	P > 0.05
Insufficient	4 (4.7)	4 (4.7)	2 (2.4)	10 (11.8)	
Normal	5 (5.9)	0 (0.0)	0 (0.0)	5 (5.9)	

URTI = upper respiratory tract infection; GIT troubles = Gastrointestinal tract troubles; Congested HTM = Congested hyperemic tympanic membrane; Bulge TM = Bulge tympanic membrane; Perf with discharge = Perforation with discharge.

Table 3 revealed that patients who complained of ear pain were 64 (75.3%). These patients were distributed as follows: 24 (28.2%) patients with deficient level of vitamin D, 38 (44.7%) patients with insufficient level of vitamin D, and only 2 (2.4%) patients with normal level of vitamin D. There is no statistical significance between values ( $p > 0.05$ ). Patients who complained of fever were predominant 48 (56.5%) among patients with insufficient level of vitamin D, followed by patients of deficient level of vitamin D with 23 (27.1%), ( $p > 0.05$ ) as shown in Table 3.

Upper respiratory tract infections were found more in patients suffered by insufficient level of vitamin D with 31 (36.5%) followed by patients suffered by deficient level of vitamin D with 20 (23.5%), ( $p > 0.05$ ). Table 3 also shows the patients who complained of irritability and crying were more in patients suffered by insufficient level of vitamin D with 15 (17.6%), ( $p > 0.05$ ). Gastrointestinal tract troubles were found more among patients suffered by insufficient level of vitamin D with 15 (17.6%).

**Table 3: Distribution of otitis media symptoms related to levels of vitamin D (n=85)**

Variables	Level of vitamin D			Total	P-Value
	Deficient No (%)	Insufficient No (%)	Normal No (%)		
<i>Pain:</i>					
Yes	24 (28.2)	38 (44.7)	2 (2.4)	64 (75.3)	P > 0.05
No	4 (4.7)	14 (16.5)	3 (3.5)	21 (24.7)	
<i>Fever:</i>					
Yes	23 (27.1)	48 (56.5)	5 (5.9)	76 (89.4)	P > 0.05
No	5 (5.9)	4 (4.7)	0 (0.0)	9 (10.6)	
<i>URTI:</i>					
Yes	20 (23.5)	31 (36.5)	2 (2.4)	53 (62.4)	P > 0.05
No	8 (9.4)	21 (24.7)	3 (3.5)	32 (37.6)	
<i>IRRITCRY:</i>					
Yes	4 (4.7)	15 (17.6)	3 (3.5)	22 (25.9)	P > 0.05
No	24 (28.2)	37 (43.5)	2 (2.4)	63 (74.1)	
<i>GIT troubles:</i>					
Yes	4 (4.7)	15 (17.6)	3 (3.5)	22 (25.9)	P > 0.05
No	24 (28.2)	37 (43.5)	2 (2.4)	63 (74.1)	

Deficient = < 20 ng/ml; Insufficient = 20 - 32 ng/ml; normal = 33 - 100 ng/ml  
URTI = upper respiratory tract infection; IRRITCRY = irritability and crying;  
GIT troubles = Gastrointestinal tract troubles.

Table 4 shows the otoscopic findings related to level of vitamin D among the study patients. Congested hyperemic tympanic membranes were found among 43 (50.6%) patients and they were distributed as follows: 17 (20%) cases of patients suffering of deficient level of vitamin D, 22 (25.9%) cases of patients suffering of insufficient level of vitamin D and 4 (4.7%)

cases among patients with normal levels of vitamin D.

Bulge tympanic membrane was predominance in patients suffered by insufficient level of vitamin D with 18 (21.2%) also, perforation with discharges were more common in patients suffered by insufficient levels of vitamin D with 12 (14.1%), ( $p > 0.05$ ).

**Table 4: Relation between otoscopic findings with level of vitamin D**

Variables	Level of Vitamin D			Total No (%)	P-value
	Deficient No (%)	Insufficient No (%)	Normal No (%)		
<i>Otoscopy findings:</i>					
Congested HTM	17 (20.0)	22 (25.9)	4 (4.7)	43 (50.6)	P > 0.05
Bulge TM	10 (11.7)	18 (21.2)	1 (1.2)	29 (34.1)	
Perf with discharge	1 (1.2)	12 (14.1)	0 (0.0)	13 (15.3)	
<b>Total</b>	<b>28 (32.9)</b>	<b>52 (61.2)</b>	<b>5 (5.9)</b>	<b>85 (100.0)</b>	

Deficient = < 20 ng/ml; Insufficient = 20 - 32 ng/ml; normal = 33 - 100 ng/ml

Congested HTM = Congested hyperemic tympanic membrane; Bulge TM = Bulge tympanic membrane; Perf with discharge = Perforation with discharge.

Seventy (82.3%) of the patients had a deficient vitamin D level followed by patients with insufficient vitamin D level 10 (11.8%) then patients with normal level of vitamin D 5 (5.9%), as shown in Table 5 and Figure 2.

We observed that the recurrent attacks of acute otitis media in the deficient group represented with three times recurrent attacks 26 (30.5%) followed by four times recurrent attacks 19 (22.4%), twice times recurrent attacks 14 (16.4%), then five times attacks 10 (11.8%) and one time of recurrent attack with 1 (1.2%), Table 5 and Figure 2.

In the group insufficient (level of vitamin D between 20 and 32 ng/ml) we found none recurrent acute otitis media only in 1 (1.2%) patient, one time in 5 (5.9%) patients and twice time in 4 (4.7%) patients.

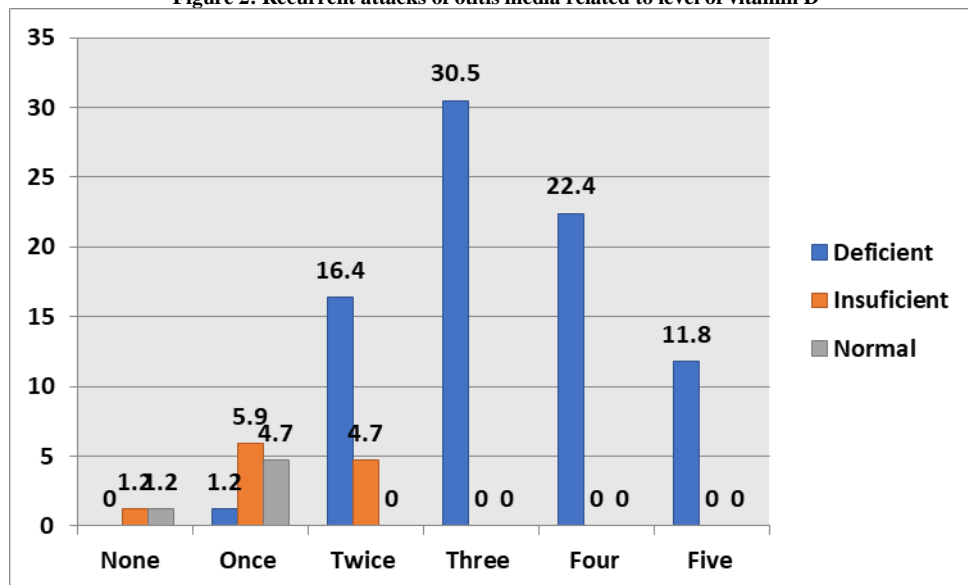
In the group of normal there was of none recurrent acute otitis media only in 1 (1.2%) patient and one recurrent acute otitis media were in 4 (4.7%) patients. Highly significant differences were found between recurrent attacks and abnormal level of vitamin D ( $p = 0.000$ ) as appeared in Table 5.

**Table 5: Distribution of recurrent otitis media related to levels of vitamin D (n=85)**

Variables	Level of vitamin D			Total No (%)	P-value
	Deficient No (%)	Insufficient No (%)	Normal No (%)		
None	0 (0.0)	1 (1.2)	1 (1.2)	2 (2.4)	P = 0.000
Once	1 (1.2)	5 (5.9)	4 (4.7)	10 (11.8)	
Twice	14 (16.4)	4 (4.7)	0 (0.0)	18 (21.1)	
Three	26 (30.5)	0 (0.0)	0 (0.0)	26 (30.5)	
Four	19 (22.4)	0 (0.0)	0 (0.0)	19 (22.4)	
Five	10 (11.8)	0 (0.0)	0 (0.0)	10 (11.8)	
<b>Total</b>	<b>70 (82.3)</b>	<b>10 (11.8)</b>	<b>5 (5.9)</b>	<b>100 (100)</b>	

Deficient = < 20 ng/ml; Insufficient = 20 - 32 ng/ml; normal = 33 - 100 ng/ml

Figure 2: Recurrent attacks of otitis media related to level of vitamin D



## DISCUSSION

Acute otitis media refers to acute inflammation of the middle ear; it is the most common infection in childhood [12] and may be due to bacteria such as pneumococci, or to viruses.

Recent studies related to serum vitamin D showed that vitamin D might play a strong immunomodulatory role in improving the incidence and severity of bacterial and viral infections. [3] In addition, several studies suggested that children with low serum vitamin D levels suffer from respiratory infectious diseases at a high risk. [4-9] Theoretically, the lack of vitamin D could cause an increased risk of recurrent acute otitis media. [13]

Our study comprised 85 patients with acute otitis media. They were (51.8%) males and (48.2%) females and male: female ratio was 1.1:1).

In the present study, acute otitis media seems to occur significantly more often in males than in females. Different prospective series [14-16] showed that the total number of episodes of acute otitis media and the number of episodes of recurrent otitis media are indeed higher in male subjects. [17]

According to Stenstrom et al. [16] study, 61% of the otitis-prone group were male children and 35% female, while other series could find no sex differences. [9] The reasons for

this sex predominance are not well known. [17]

In the present study, we found the age of the patients ranged between 1 to 15 years and the mean age of all patients was  $5.6 \pm 2.8$  years.

We noted that most of the patients were between the age 1 to 5 years (56.5%). Also, we found in our study that fever symptom of acute otitis media represented (56.5%) in the age group 1 – 5 years old, followed by the age group 6 – 10 years old with (32.9%). The difference between values is statistically significance ( $p = 0.000$ ). The ear pain was among all age groups. It was predominant in the age group 6 – 10 years with (36.5%) followed by patients of age group 1 – 5 years with (31.8%), ( $p < 0.05$ ).

URTI in the age group 6 – 10 years old was higher than in other age groups with (30.6%). Irritability and crying found among patients age group 1 – 5 years of (25.9%), and similar to this finding was the variable of gastrointestinal tract troubles ( $p$ -value  $< 0.05$ ).

Liese et al. [18] reported in their study, that the most common sign or symptom was redness of the tympanic membrane (52.8%) of episodes, and ear pain (48.4%) of episodes. Ear discharge was reported for (14.4%) of episodes. They reported, no differences were observed in documented

symptoms of acute otitis media by age group.

Most cases of acute otitis media occurred in young children ages 6 to 24 months, with the incidence of acute otitis media declining significantly after age 5 years. <sup>[19,20]</sup> A 2005 global disease burden modeling-based study estimated the annual incidence of acute otitis media as follows: children under age 5 years, 45 to 60 percent; children aged 5 to 14 years, 19 to 22 percent. <sup>[21]</sup>

We found in our present study, otoscopic findings were bulge tympanic membrane, congested hyperemic tympanic membrane and perforation with discharge. In the age group 1-5 years old we found congested hyperemic tympanic membrane (43.5%) followed by the bulge tympanic membrane (9.4%) and discharge with perforation (3.5%). Additionally, in the age group 6 – 10 years old, the bulge tympanic membrane was predominant (18.8%), followed by discharge with perforation (10.6%). In addition, in the age group 11 – 15 years old the bulge tympanic membrane was predominant (5.9%). Highly significant differences were found between otoscopic findings and the age groups ( $p = 0.000$ ).

Recurrent attack of acute otitis media seems to be higher in the age group 1 – 5 years old than that in the age group 6 – 10 years old and the age group 11 – 15 years old. Significant differences were found between recurrent attacks and the age groups ( $p = 0.041$ ).

The abnormal levels of serum vitamin D (deficit, insufficient), seem to be higher in the age group 1 – 5 years old than in the other age groups. No significant differences were found between levels of vitamin D and the age groups ( $p > 0.05$ ).

A case-control study was done on 169 children in Turkey with age range between 1–13 years and the mean age was  $(6.20 \pm 3.27)$  years. The study was on vitamin D deficiency in children with acute otitis media and reported that there is correlation between vitamin D deficiency and acute otitis media. <sup>[22]</sup>

APRISMA-compliant meta-analysis and systematic review was done regarding association between vitamin D and development of otitis media cross-sectional study. Of the 89 articles identified by database search, five studies reported data of 16 689 individuals who were included in meta-analysis and reported that the plasma vitamin D level might play an important role on the progression of acute otitis media. <sup>[13]</sup>

Sabetta et al. <sup>[23]</sup> stated that a vitamin D level of more than 30 ng/ml significantly ( $P < 0.0001$ ) reduces the risk of respiratory tract infections.

A randomized clinical trial was done on 116 children in Italy complaining of acute otitis media and 58 were treated with vitamin D and 58 children were treated with placebo and mean age ( $33.7 \pm 11.7$  months) from 1 to 5 years and reported that there is a relationship between acute otitis media and vitamin D supplementation. The results have shown that the intervention reduced the number of acute otitis media episodes in the vitamin D group during the 4-month study period, in comparison with the placebo. <sup>[3]</sup>

A cross-sectional study included 74 children to elaborate the relation of vitamin D level and Otitis media with effusion, Asghari et al <sup>[24]</sup> reported lower serum levels of vitamin D in Otitis media with effusion patients.

Hundred twenty children with Otitis media with effusion were enrolled in a case-control study by Hosseini et al. <sup>[25]</sup> They reported that there was not a significant relation shown between vitamin D levels in children and Otitis media with effusion.

Salem et al. <sup>[26]</sup> reported that both vitamin D deficiency and insufficiency were significant in children suffering from acute otitis media than normal children and abnormal levels of vitamin D are more in the younger age group of children from 1 to 6 years than the older children from 7 to 13 years. Cayir et al. <sup>[11]</sup>, reported in their study, that a relation between recurrent attack of AOM and vitamin D deficiency in the study group than the control group. Our

study agrees with them, but Salem et al. [26] did not report a significant relation between low vitamin D levels and the recurrence of acute otitis media.

In our present study, the patients who complained of ear pain were (75.3%). These patients distributed as follows: (28.2%) patients with deficient level of vitamin D, (44.7%) patients with insufficient level and only (2.4%) patients with normal level. There is no statistical significance between values ( $p > 0.05$ ).

Patients who complained of fever were predominant (56.5%) among patients with insufficient level of vitamin D, followed by patients of deficient level with (27.1%), ( $p > 0.05$ ).

Upper respiratory tract infections were found more in patients suffered by insufficient level of vitamin D of (36.5%) followed by patients suffered by deficient level of (23.5%), ( $p > 0.05$ ).

Many studies have demonstrated the correlation between vitamin D deficiency and the occurrence of respiratory tract infections. Moreover, vitamin D supplementation has decreased the occurrence of acute otitis media, Otitis media with effusion, and other upper respiratory tract infections. [27,28]

## CONCLUSION

Our study showed relation between abnormal level of vitamin D and recurrent acute otitis media mostly in the age group from 1-5 years due to difficult economic situation in Yemen because the long period of war more than seven years lead to malnutrition among children.

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**Conflict of Interest:** None

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**Ethical Approval:** Approved

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