

Vitamin D levels in children diagnosed with acute otitis media

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Objective

To investigate the relationship between acute otitis media (AOM) and vitamin D level in children.

Patients and methods

This prospective study was conducted at Assiut University Hospital between December 2016 and March 2017. The study group comprised ambulatory children who were diagnosed with AOM and healthy controls. The blood sample (5 cm) was taken immediately after the diagnosis of AOM in the laboratory for measuring serum 25-hydroxyvitamin D. Abnormal value=deficiency+insufficiency.

Results

Of the 40 children included in this study, 30 were the cases and 10 were controls. The mean age of the cases was 4.92 ± 3.08 and 5.92 ± 4.04 years for the controls besides 18 (60%) of the AOM group were boys and 12 (40%) were girls, compared with five (50%) boys and five (50%) were girls in the control group. Otagia and congested tympanic membrane were present in all children of the diseased group. Also 70% had upper respiratory tract infection preceding the attack of AOM and 33.3% had previous attack of AOM. Twenty-two (73.3%) out of 30 children of the AOM group have an abnormal value of vitamin D and it was statistically significant than the control group.

Conclusion

Both vitamin D deficiency and insufficiency were significant in children suffering from AOM than normal children.

Keywords:

acute otitis media, vitamin D, children

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Introduction

The incidence of acute otitis media (AOM) rises in winter when the upper respiratory tract infections (URTIs) are common. The incidence of otitis media depends on a combination of several factors, particularly a condition in which sensitivity to Eustachian tube dysfunction and recurrent respiratory tract infection rises [1].

The presence of vitamin D receptors in several tissues suggest that vitamin D may play a role in the etiopathology of diseases [2,3].

Vitamin D receptors have been described in all immune system cells, particularly cells producing antigens, such as active T and B lymphocytes, active macrophages, and dendritic cell. Accordingly, there is accumulating evidence that consumption of vitamin D may reduce respiratory tract infection susceptibility in children [4–6].

Several studies have reported a correlation in children between low or inadequate vitamin D concentrations and respiratory tract infections since vitamin D is not

just a vitamin; it improves efficacy of the immune system [7,8].

The aim of the study is to investigate the relationship between AOM and vitamin D level in children.

Patients and methods

Study patients

This is a case–control study conducted at the Department of Otorhinolaryngology at Assiut University Hospital between December 2016 and March 2017 after obtaining approval from the institutional ethics committee and informed consent from the parents of all children in the study. The study group comprised ambulatory children who were diagnosed with AOM and healthy controls.

Age of children from 1 to 13 years.

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- (1) Group A:
 - (a) Thirty children diagnosed with AOM by history, examination, and otoscopic examination.
- (2) Group B:
 - (a) Ten healthy controls children free from any craniofacial abnormality or chronic diseases.

Inclusion criteria

The criteria of diagnosis of AOM is:

- (1) Acute onset.
- (2) Inflammatory signs or symptoms (otalgia, tympanic membrane hyperemia).

Exclusion criteria

- (1) Craniofacial anomalies.
- (2) Rickets.
- (3) Chronic medical diseases.

The case and control groups are matched for age and sex.

Every case was subjected to the following:

- (1) History taking:

Concerning symptoms related to AOM.

 - (a) Pain.
 - (b) Fever.
 - (c) URTIs.
 - (d) History of similar attacks of AOM.
 - (e) Irritability.
 - (f) Continues crying.
 - (g) Decreased appetite.
 - (h) Lack of sleep.

Clinical examination: full ENT examination

Ear examination:

- (1) Tympanic membrane is congested bulging

The patient in whom otoscopic examination presented inconsistency or ambivalence, visual otoscopy was reperformed by another otolaryngologist. In case of continuing the inconsistency or ambivalence, the patient was excluded from the study.

AOM is diagnosed on the basis of the criteria being met: acute onset, inflammatory signs, or symptoms (otalgia, severe tympanic hyperemia). Documented visit records including name of the child, date of the visit, and symptoms taken from the parents.

Laboratory investigation

Blood samples (5 cm) were taken immediately after the diagnosis of AOM in the laboratory for measuring serum 25-hydroxyvitamin D [25(OH)D].

Specimen collection and handling for vitamin D:

- (1) Serum used for the assay collect the whole blood by a venipuncture and allow clotting.
- (2) The blood sample was intubated at 37°C for 20 min and for long-term storage they can be stored at -20°C until analysis.

Principle of the test

- (1) The kit is a solid phase enzyme-linked immunosorbent assay, based on the principle of competitive binding. Antivitamin D antibody coated well are incubated with vitamin D standards, controls samples, and vitamin D-biotin conjugate at room temperature for 90 min.
- (2) Serum 25(OH)D was done on an enzyme-linked immunosorbent assay reader.
- (3) Levels between 30 and 100 ng/ml were regarded as normal.
- (4) Levels between 10 and 30 ng/ml were considered as vitamin D insufficient.
- (5) Levels below 10 ng/ml were categorized as vitamin D deficient.

Statistics

The statistical package for the social sciences version 16 (SPSS Inc., Chicago) was used for data analysis. Quantitative variable will be expressed as mean±SD and qualitative variable will be expressed as number and percentage. To compare the results between the two groups aspired sample independent *t*-test was used, and qualitative variables were compared by χ^2 and Fisher's exact tests. *P* value less than 0.05 was considered as significant.

Results

Of the 40 children included in this study, 30 were the cases and 10 were controls. The mean age of the cases was 4.92±3.08 and 5.92±4.04 years for the controls. Besides, 18 (60%) of the AOM group were boys and 12 (40%) girls, compared with five (50%) boys and five (50%) were girls in the control group.

All 30 children who were diagnosed complaint of ear pain and by examination tympanic membrane was congested in all of them. Of these, 70% had URTI preceding the attack of AOM and 33.3% had previous attack of AOM (Tables 1–4).

It was noted that vitamin D deficiency and insufficiency is statistically significant in the AOM group than the control group (Fig. 1).

Table 1 Clinical presentation of the acute otitis media group

	Acute otitis media [N (%)]
Pain	30 (100.0)
Fever	13 (43.3)
Upper respiratory tract infection	21 (70.0)
Recurrence	10 (33.3)
TM (congested)	30 (100.0)

TM, tympanic membrane.

Table 3 Values of vitamin D in the control group

	Control		Normal
	Range	Mean±SD	
Vitamin D	7.9–37	24.82±11.74	30–100 ng/ml

Twenty-two (73.3%) out of 30 children of the AOM group have abnormal value of vitamin D and is statistically significant than the control group as in Table 5 and Fig. 2.

Abnormal value=deficiency+insufficiency.

Abnormal levels of vitamin D in relation to age, sex, URTI, and recurrence. It was observed that the abnormal level of vitamin D is statistically significant in the younger age group 1–6 years than the older age group 7–13 years and statistically significant in children who had URTI and no relation to recurrence of AOM infection and sex (Table 6).

Discussion

AOM is one of the most common diseases in children and the most frequent reason for antimicrobial prescriptions. It is currently acknowledged that AOM is a bacterial complication of viral URTI. About 35% of upper respiratory infection episodes are complicated by AOM, occurring mainly within the first week of upper respiratory infection onset [9,10].

The microbial etiology for AOM includes additional pathogens for which there is no vaccine available, including nontypeable haemophilus influenzae, nonvaccine types of *Streptococcus pneumoniae* and *Moraxella catarrhalis* and *Streptococcus pyogenes* and *Staphylococcus aureus*. Therefore, there is continuous search for alternative ways to prevent AOM, Otitis media with effusion (OME), and Chronic otitis media with effusion (COME). In recent years, vitamin D has been suggested to boost immunity and provide a preventive measure against various infectious conditions, including respiratory tract infections [11].

The activation of 25(OH)D into the active 1,25(OH)D occurs by enzymatic conversion in the kidneys by CYP27B1, and this enzyme is also expressed in many

Table 2 Values of vitamin D in the acute otitis media group

	Acute otitis media		Normal
	Range	Mean±SD	
Vitamin D	5.9–85	23.37±16.27	30–100 ng/ml

Table 4 Laboratory data for vitamin D in acute otitis media and control groups

	Vitamin D [N (%)]		P value
	Acute otitis media	Controls	
Normal	8 (26.6)	4 (40)	0.248
Insufficiency	11 (36.7)	3 (30)	0.033*
Deficiency	11 (36.7)	3 (30)	0.033*
Total	30 (100)	10 (100)	

According to statistical analysis, comparison 25-hydroxyvitamin D levels in the study group versus control group. * $P < 0.05$, significant using the χ^2 -test.

other cells in the body, including epithelial cells and macrophages. This insight has spurred a lot of research interest into the potential extraskeletal effects of vitamin D. Vitamin D induces the expression of antimicrobial peptides in epithelial cells and in macrophages and dampens inflammation by downregulating proinflammatory cytokines [12].

In cases of vitamin D deficiency, proinflammatory cytokines increase, immune response is disturbed, leukocyte chemotaxis is affected, and tendency to infections rises [2,6].

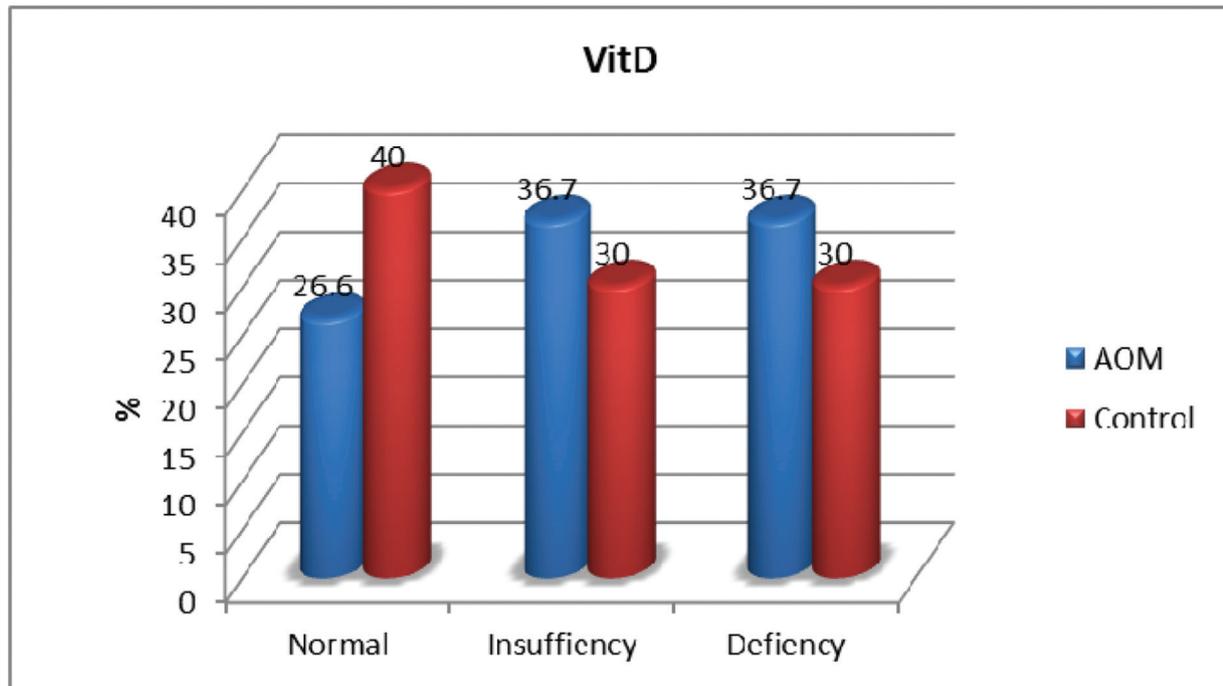
In several studies, the role of vitamin D deficiency has been proven in respiratory and middle ear infections [13,14].

In 2014, the case-control study was done on 169 children in Turkey with a mean age 1–13 (6.20 ±3.27) on vitamin D deficiency in children with AOM and reported that there is correlation between vitamin D deficiency and AOM [15].

In 2016, 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 AOM [16].

In our study it was found that vitamin D deficiency and insufficiency is statistically significant in children with AOM and abnormal levels (deficiency+insufficiency) are significant in those children. Abnormal levels of vitamin D are more in the younger age group of

Figure 1



The percentage of serum vit. D (normal, insufficiency and deficiency) in acute otitis media and control group.

Table 5 Comparison between normal and abnormal value of vitamin D in acute otitis media and control group

	Group [N (%)]		P value
	Acute otitis media	Control	
Vitamin D			
Abnormal	22 (73.3)	6 (60.0)	0.002
Normal	8 (26.7)	4 (40.0)	0.248

children from 1 to 6 years than the older children from 7 to 13 years. There is no relationship between abnormal levels of vitamin D and sex of the child. Abnormal levels of vitamin D are statistically significant in AOM preceded by URTI.

Cayir *et al.* [15], in their case-control study reported a relation between recurrent attack of AOM and vitamin D deficiency in the study group than the control group. But in our study, we did not report a significant relation between low vitamin D levels and the recurrence of AOM.

Sabetta *et al.* [17] stated that a vitamin D level of more than 30 ng/ml significantly ($P < 0.0001$) reduces the risk of respiratory tract infections.

In 2013, randomized clinical trial was done on 116 children in Italy complaining of AOM and 58 were treated with vitamin D and 58 children were treated with placebo and mean age (33.7 ± 11.7) month from 1 to 5 years and reported that there is a relationship

between AOM and vitamin D supplementation. The results have shown that the intervention reduced the number of AOM episodes in the vitamin D group during the 4-month study period, in comparison with the placebo [14].

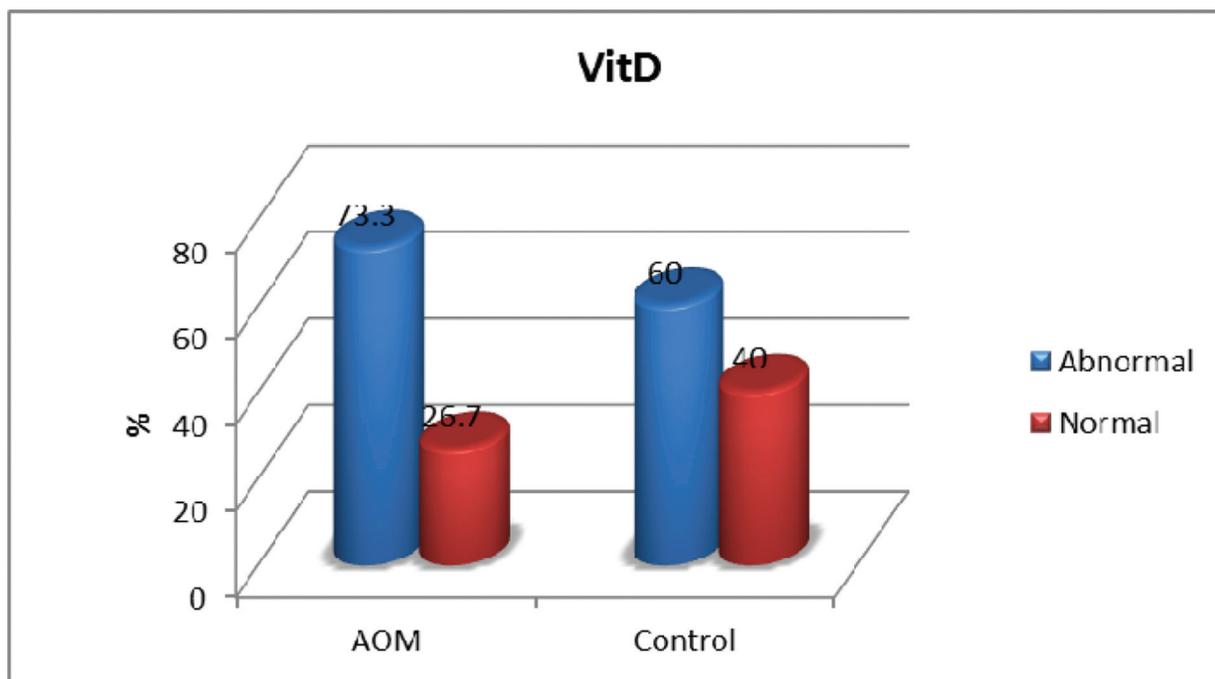
In 2017, a cross-sectional study included 74 children to elaborate the relation of vitamin D level and OME, Asghari *et al.* [18] reported lower serum levels of vitamin D in OME patients.

In 2016, 120 children with OME were enrolled in a case-control study by Hosseini *et al.* [19]. They reported that there was not a significant relation shown between vitamin D levels in children with OME.

One hundred and seventy-four children with otitis media with effusion and 80 control patients were included in the study of Akcan *et al.* [20]. This study not only shows the relationship between vitamin D and otitis media with effusion development, but also demonstrates the effects of vitamin D on otitis media with effusion prognosis. There is a significant association between 25(OH)D deficiency and follow-up outcomes of otitis media with effusion.

A study published in *Acta Paediatrica* by Walker *et al.* [21] hypothesized that higher serum concentrations of 25(OH)D would be associated with a reduced risk of COME.

Figure 2



The percentage of normal and abnormal (insufficiency & deficiency) value of vit. D in acute otitis media and control group.

Table 6 Table 6: Abnormal level of vit D in acute otitis media group in relation to child age, sex, previous upper respiratory tract infection and recurrence of acute otitis media

	Abnormal vitamin D acute otitis media [N (%)]	P value
Age		
Younger age (1–6)	17 (77.3)	0.001
Older age (7–13)	5 (22.7)	
Mean±SD	5.14±3.07	0.767
Sex		
Male	13 (59.1)	0.690
Female	9 (40.9)	
Upper respiratory tract infection	17 (77.3)	0.001
Recurrence	9 (40.9)	0.057

The biological mechanism underlying the potential role of vitamin D in COME has not been fully established. It is quite possible that vitamin D plays a role in preventing AOM, which is caused by microbes, and thus subsequently COME, which is not caused by microbes [11].

In agreement with the previous studies there is a relationship between AOM infection and serum level of vitamin D it was found that vitamin D play an important role in the occurrence of AOM infection in our children and can share in the regimen of treatment of AOM when it found abnormal. This would provide a simple, safe, and potentially beneficial way to strengthen the mucosal immunity

of these children, which could lead to a better clinical outcome in AOM.

Conclusion

Our study has shown that vitamin D deficiency, insufficiency, or abnormal value (deficiency +insufficiency) are significant in children suffering from AOM than normal children.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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