

Humoral Immunity and Audiological Findings in Children with Vertigo

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Abstract: In a study of a school aged population 15% of children were found to have experienced at least 1 episode of vertigo in the previous year, the differential diagnostic process is extensive in children with vertigo and correct diagnosis requires otologic examination, audiological evaluation as well as neurological and general physical examination. There are numerous hypotheses regarding the etiology and pathology of vertigo, including a suggested role for immune dysfunction. While immune system abnormalities have been reported in children with vertigo with reduced immune function. Objective: To determine the main cause of vertigo in those children they visited Pediatric and ENT clinics during 2011 and evaluate humoral immunity of children through evaluation of serum antibody level of immunoglobulin (IgG-IgM-IgA) and compared with the healthy control children. Methods: The study was carried out in the ENT, audiology and pediatric departments in El- Zahraa hospital on 30 children with vertigo (18 males and 12 females) the age range (5– 12 years) and 20 healthy children as control group, age range (4-13years) to evaluate hearing and determine the serum level of IgG, IgM and IgA by ELISA method. Results: Otitis media with effusion, migraine- associated dizziness, vestibular neuronitis and Benign paroxysmal vertigo of childhood, all causes of vertigo had significantly lower serum level of IgG, IgM and IgA compared to control children ($p < 0.001$). Conclusion: Children with vertigo had significantly reduced level of serum IgG, IgA and IgM compared to control children suggesting the defect in the immune function. So we recommend farther investigations to detect the level of immunoglobulin in the middle ear effusion.

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1. Introduction

Vertigo in children is a diagnostic challenge for clinicians because of their immature peripheral and central vestibular systems and limited communication abilities (1, 2). When it manifests it has a different clinical picture than in adults. Meniere's syndrome is rare in children, while benign paroxysmal vertigo of childhood and other migraine equivalents are more common than in adults. Benign paroxysmal vertigo of children (BPVoC) occurs very seldom in children because cupular deposits are a phenomenon of the aging vestibular labyrinth (3). Brainstem and cerebellar tumors are relatively more common in children than in adults (4). Vertigo in children as in adults is often divided into peripheral and central causes. Peripheral causes include otitis media-related vertigo, BPVoC, Meniere's disease, Posttraumatic vertigo, perilymphatic fistula, vestibular neuronitis and labyrinthitis (2). Migraine-related vestibulopathy: often occurs in patients with a personal or family history of migraine. It is one of the most common causes of vertigo and dizziness. There are different theories for the pathophysiology of migraine-associated vestibulopathy. These include a spreading, global central nervous system (CNS) depression to account for central findings, and vasospasm of the

internal auditory artery to account for peripheral cochleovestibular symptoms(5).

Others attribute the central and peripheral symptoms to deficits in the release of neuropeptides during an attack. In a study of school aged population, many children complaint of vertigo, many related to movement of head ophthalmologist consultation is beneficial. The most common reason for dizziness in children is benign paroxysmal vertigo of childhood (BPVoC) and migraine associated dizziness also otitis media-related dizziness. (BPVoC) is not induced by head positioning (6).

There have been numerous finding of altered immune function in vertigo and also numerous attempts at determining susceptibility genes including humane related genes may be associated with vertigo. In addition, a number of studies have reported that a common variable immunodeficiency (CVID) comprises a heterogeneous group of disorders characterized by hypogammaglobulinemia, defective specific antibody production, and increased susceptibility to recurrent and chronic infection (7). Patients with CVID more frequently have autoimmune disorders (8).

The aim of the present study is to evaluate the role of humeral immune system in children suffered

from vertigo through evaluation of immunoglobulin (IgG, IgM and IgA) in relation to different causes of vertigo.

2. Methods:

This study included 30 children patients with vertigo 18 males and 12 females age range (5-12years) and 20 healthy children age range(4-13years)as a control. These patients were selected from ENT and pediatric out patient's clinic of El Zahraa hospital, Al Azhar University. Most children were seen as outpatients and only a few needed hospitalizations. We collected information on the nature of the symptoms (acute or chronic, paroxysmal or continuous, attack severity and number and duration of attacks). Provocative factor ear symptoms, head traumas and other diseases, we also collected data when available on laboratory and other specialties: - neurologic – ophthalmologic and psychiatric. We also need to know more about medical history, current medication and family history.

Children with known endocrine, cardiovascular, pulmonary, liver or kidney diseases were excluded from the study. To diagnose children with vertigo careful history taken according to Dizziness Handicap Inventory (25) audiogram, tympanometry were done and if not diagnostic magnetic resonance imaging or computed tomographic scans should done.

Laboratory investigation:

The blood samples were taken before the start of any treatment. Complete blood count including cell count for major immune cell population i.e. neutrophil, lymphocytes, eosinophilis, monocytes and platelets. Other routine laboratory tests including liver function, kidney function and fasting blood sugar were done for all children. Serum antibodies levels of immunoglobulin (IgG, IgM and IgA) were assayed in all children.

Five ml of venous blood sample were taken from patients and control subjects under complete aseptic condition and divided into: 2ml were put in EDTA vacutainer for CBC to be done on coulter MD18 automated hematological counter. 3 ml were taken in plain vacutainer. they were left to clot, centrifuged and sera were separated for protein laboratory investigations (liver and kidney functions) to be done on Cobas c311 auto analyzer and the rest of the samples were separated and stored at -20 C till the time of the assay of the IgG, IgM and IgA which is based on enzyme linked immune sorbent assay (ELISA) technique using Assay Max Human for IgG ELISA kit with cat. No. EI7200-1, IgM ELISA kit with cat. No. EI7300-1 and for IgA ELISA kit with cat. No. EI7001-1.

The test principle: a polyclonal antibodies

specific for IgG, IgM, and IgA has been pre-coated onto a 96-well micro plate with removable strips. Immunoglobulin in standard and sample is sandwiched by the immobilized antibodies and the biotinylated poly clonal antibody specific for each immunoglobulin is recognized by a streptavidin peroxidase conjugate. All unbound material is then washed away and a peroxidase enzyme substrate is added. The colour developed is stopped and the intensity of the colour is measured.

Statistical analysis:

Data were computerized using SPSS (version 11.5) with descriptive analysis and correlation of data, frequencies, ranges mean and standard deviation were calculated. Tests of significance using Chi-square test with significance level <0.05 were used.

3. Results:

Our study group of 30 children (18 males, 12 females) range age from 5-12 years, mean age 10.5 years was little less than 1% all children visiting the ENT clinic during 2011, the mean age at most of symptoms was around 9 years. Age of onset of vertigo peaked from 8-12 years. The most common causes of vertigo are benign paroxysmal vertigo of childhood, migraine associated dizziness, otitis media-related dizziness, vestibular neuronitis and the distributions of diagnosis are shown in table (1).

Table (1): Frequency distribution of tympanometric finding and suggestive causes of vertigo among cases

Causes of Vertigo	Tympanometric data types A, B or C	Number of children
Otitis media related dizziness	Type B	9 (30%)
Migraine associated vertigo	Type A	6 (20%)
BPVoC	Type A	4 (13.3%)
Vestibular neuronitis	Type A	3 (10%)
Psychogenic vertigo	Type A	2 (6.6%)
labyrinthitis	Type A	1 (3.3%)
Post traumatic	Type B	1 (3.3%)
Post operative	Type B	1 (3.3%)
Sinus related vertigo	Type C	1 (3.3%)
Epilepsy	Type A	2 (6.6%)

Table (1): It was noted that all cases showed type (A) tympanogram except (30%) cases of otitis media, (3.3%) case post-traumatic and (3.3%) case post-operative showed type (B) tympanogram while sinus related vertigo showed type(C) tympanogram. Also (6.6%) cases psychogenic and (6.6%) cases diagnosed as epilepsy by EEG and shows temporepaital epileptogenic focus.

Table (2): Pure tone audiometry:

Frequencies	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz
Vertigo						
BPPV	15 ± 5	15 ± 5	10 ± 10	10 ± 5	5 ± 5	5 ± 5
Migraine V	15 ± 5	15 ± 5	10 ± 5	10 ± 5	5 ± 5	5 ± 5
V. neuronitis	15 ± 5	15 ± 5	5 ± 5	5 ± 5	10 ± 5	5 ± 5
OM related dizziness	30 ± 5	25 ± 5	20 ± 5	10 ± 5	10 ± 5	5 ± 5
Psychogenic vertigo	10 ± 5	10 ± 5	10 ± 5	5 ± 5	5 ± 5	5 ± 5
labyrinthitis	15 ± 5	10 ± 5	10 ± 5	25 ± 5	35 ± 5	40 ± 5
Posttraumatic	50 ± 5	40 ± 5	20 ± 5	20 ± 5	30 ± 5	30 ± 5
Postoperative	30 ± 5	25 ± 5	20 ± 5	20 ± 5	15 ± 5	15 ± 5
Sinus related Vertigo	20 ± 5	20 ± 5	10 ± 5	10 ± 5	5 ± 5	5 ± 5

It was noted that all cases showed normal pure tone audiometry except in cases of vertigo due to otitis media showed mild CHL and case of post traumatic HL showed moderate CHL due to

longitudinal temporal bone fracture. Also, the case of labyrinthitis due to viral infection showed mild SNHL (table2).

Table (3): Significant difference between cases and controls regarding means of studied immunological variable (n=50)

Serologic variables ng/ml	Cases	Controls	f-test	P value (sig)
	Mean± SD	Mean± SD		
IgM	78.833±15.691	96.400±22.039	10.859	.002**
IgG	835.17±89.828	1011.60±240.314	13.468	.001
IgA	69.4000±14.26740	96.8000±14.19266	44.442	.000**

** Correlation is significant at the 0.01 level (2-tailed) between serum IgM & and IgA.

Table (4): Distribution of cases according to audiological and serologic finding:

Audiogram	Ig G	Ig M	IgA
	Mean± SD	Mean± SD	Mean± SD
Normal audio	842.25±87.142	80.375±16.756	68.187±12.528
mild CHL	754.50±91.217	64.000±19.798	75.500±13.435
mild SNHL	837.50±67.175	91.000±15.556	70.500±4.949
Moderate CHL	853.50±118.675	73.750±12.038	61.250±17.346

Table (4) shown the distribution of cases according to audiogram results and serologic indicators (n=30). Children with vertigo had significantly reduced level of serum IgG, IgA and IgM as compared to control children suggesting the defect in the immune function.

4-Discussion:

Vertigo is disorder that affects about 5 in ten thousands of children worldwide 5/10.000 with ratio of males / females 2:1 it has been known that extensive interaction occur between the immune system and neural system/brain, and that normal neuro-development is contingent upon an appropriate interaction with the immune system. Patient medical history was the most important diagnostic tool and information about family history.

Benign paroxysmal vertigo of children (BPVoC) defined as at least three transient episodes of vertigo of the child or of the environment, severe enough to interfere with normal activities and not associated

with loss of consciousness or neurological deficits. Altogether 2% of children fulfilled these criteria (9). According to Dizziness Inventory Questionnaire and Basic Audiological evaluation the causes of vertigo were clarified as shown in table (1).

In our study 4 cases (13.3%) diagnosed as BPVoC which is agree with the previous study (10) who said that BPVoC is a vestibular disorder characterized by sudden brief episodes of spinning vertigo, rarely lasting more than a few minutes many times per day to few times per month. During the attack the child is conscious and often frightened, afterwards continuing to play as though nothing happened. Pallor is frequently associated with the attack. The attacks may occur in any position and are not provoked by head posture or movement. Typical age of onset is the first 4 year of life, soon after onset the attacks become more frequent, then gradually decreasing and disappearing around the age of 10 years (10). The diagnosis of BPVoC is based on a

typical clinical picture otologic, neurological examinations including audiogram, ENG, EEG are normal. There is no treatment and the attacks are self-limiting (11). It is important to inform the family of the benign course of the disorder and usually diagnosed only after the exclusion of all other known form of vertigo (12).

In our study 9 cases (30%) diagnosed as otitis media related dizziness. Grace and Pfeleiderer (13) stated that otitis media with effusion is one of the most common reasons for dizziness and vertigo in children due to pressure changes within the middle ear. Other believe that serous labyrinthitis has been suggested to be responsible for vestibular disturbances in children with OME (14). Children with severe visual impairment should be considered more vulnerable to OME sequelae as balance problems (15). Most child patients with OME completely resolve after ventilation tube insertion (16), so early intervention is important (17).

Psychogenic vertigo or dizziness is underestimated by clinicians who work with children (18), were in our study 2 child (6.6%) who's in examination fit vertigo of psychogenic origin. The most common complaints are headaches followed by dizziness, vertigo and fainting. Anxiety or depressive disorders can cause dizziness (19). These children had undergone many examinations by many different specialists. Finally a child psychiatrist confirmed diagnosis.

In our study vestibular neuronitis (10%) were diagnosed, which is agree with study done by Karlberg et al. (20), were the patients complaint vertigo aggravated by head movement with horizontal rotational nystagmus, hearing normal with general symptoms of malaise, pallor, nausea and vomiting may be present which gradually subsides within weeks or months (21).

Other causes of vertigo in the present study are Labyrinthitis, post traumatic, post operative and sinus related vertigo each of them is (3.3%). Ernst et al (22) stated that no significant correlation between the mechanism of trauma and type of neurological disorders. The diagnosis of epileptic origin of vertigo or dizziness confirmed with EEG, we had two children with epilepsy (6.6%) as diagnosed and treated in pediatric clinic.

Our work revealed significantly reduced levels of serum IgG, IgM and IgA in children with vertigo compared to the controls, suggesting an defect in immune function in vertigo the results of this study agree with obtained by (23) were he said that the immune system abnormalities may be directly related to underlying biologic processes of vertigo or may be indirect reflection of actual pathologic mechanism thus identification of the immune defect responsible

for reduced immunoglobulin production may provide common affection of neuro development, further investigation of cellular immunity projects should be done to find the relationship between immune dysfunction and the progression of behavioral and developmental change throughout the cause of vertigo.

Berkow and Robert (23) stated that Immunoglobulin deficiencies are the result of congenital defects affecting the development and function of B lymphocytes (B-cells). There are two main points in the development of B-cells when defects can occur. First, B-cells can fail to develop into antibody-producing cells. X-linked agammaglobulinemia is an example of this disease. Secondly, B-cells can fail to make a particular type of antibody or fail to switch classes during maturation. Initially, when B-cells start making antibodies for the first time, they make IgM. As they mature and develop memory, they switch to one of the other four classes of antibodies. Failures in switching or failure to make a subclass of antibody leads to immunoglobulin deficiency diseases. Another mechanism that results in decreased antibody production is a defect in T-helper cells. Generally, defects in T-helper cells are listed as severe combined immunodeficiencies (23).

Also the present study suggests that the immaturity of immune system is associated with the occurrence of vertigo. Bovo et al (24) stated that the incidence of autoimmune inner ear disease (AIED) is difficult to determine: probably it is a rare disease, accounting for < 1% of all cases of hearing impairment or dizziness. Nevertheless, the diagnosis of AIED might be overlooked because of the lack of a specific diagnostic test. The hallmark of this clinically diagnosed condition is the presence of a rapidly progressive, often fluctuating sensor neural hearing loss (SNHL) over a period of weeks to months. Vestibular symptoms, such as generalized imbalance, ataxia, positional vertigo and episodic vertigo may be present in almost 50% of patients (24).

Conclusion:

Vertigo in children is not very rare, only a fraction of these children are evaluated, many of children first seen by pediatrician or neurologist. So close cooperation between different specialties is essential for diagnosis of different causes of vertigo.

Further investigations should be done to find the relationship between immune dysfunction and vertigo.

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