Serum Immunoglobulins (IgG and IgA) Level in Chronic Sinusitis and Otitis Media Patients

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Abstract. Sinusitis and otitis media are two of the most common indications for antimicrobial agents of upper respiratory tract infection. This study was aimed to determine the effect of two chronic upper respiratory tract diseases (sinusitis and otitis media) on immunoglobulins levels via assessment the level of serum IgG and IgA in sinusitis and otitis media patients using single radial immune diffusion technique. A total of 100 sera samples were included in this study, all of them were adults, 40 samples collected from each of sinusitis and otitis media patients. Control group was included 20 samples from healthy donors. The mean of IgG concentrations in sinusitis patients (1078.6 mg/dl) revealed significant decreasing comparing with control group (1249.82 mg/dl), whereas IgG level in otitis media patients (1338.77 mg/dl) recorded non significant alteration. IgA mean of otitis media (388.26 mg/dl) significantly decreased compared to control group (235.3 mg/dl) while IgA mean of sinusitis samples (244.4 mg/dl) did not record any alteration. This study concluded that chronic sinusitis cause decreased of IgG while chronic otitis media cause increased IgA level. In general the immunoglobulins concentrations were mild moderate.

Keywords: sinusitis, otitis media, immunodeficiency, IgG, IgA and upper respiratory tract.

1. Introduction:

Upper respiratory tract infection (URTI) is a nonspecific term used to describe infections involving the paranasal sinuses, nose, pharynx and larynx (Meltzer et al., 2004). URTI are mainly infectious diseases resulting from interaction between microbes and immune response (Bentivegna et al., 2012). URTI can be placed within three major categories: rhinosinusitis, otitis media and pharingiotitis (Kenealy, 2011).

Chronic and recurrent respiratory diseases including sinusitis and otitis media have been correlated with antibody deficiencies. IgG and its subclasses deficiencies have been elucidated as a critical factor for chronic sinusitis (Chee et al., 2001).

Sinusitis is used to describe the nasal symptoms including common cold, sinusitis and nasopharyngitis (Morris, 2009). Nasal-associated lymphoid tissue is a site for humoral and cellular immune responses in the upper respiratory tract. Immunoglobulins are major elements in human adaptive immune responses and deficiencies of serum immunoglobulins may be linked to recurrent
infections (Hsin et al., 2008). In chronic sinusitis, the membranes of the nose thicken and paranasal sinuses because they are inflamed (Bachert et al., 2014). The most common immunodeficiency associated with chronic sinusitis is an IgG subclass deficiency (Quinn and Ryan, 2002).

Otitis media (OM) is a term used to describe an inflammation process within the middle ear space that is generally associated with fluid accumulation. The pathogenesis of OM is involving the innate and adaptive immune response, microbial load, eustachian tube dysfunction, genetic factors and environmental factors (Martines et al., 2010). The bacteria that most often cause OM are Streptococcus pneumonia, Moraxella catarrhalis and haemophilus influenzae (Dickson, 2014). Approximately 5-10% of these infections turn into chronic otitis media (COM) (Depreux et al., 2008). Abnormal innate or adaptive immune response may occur in the middle ear mucosa (Lin et al., 2014).

Immune response against OM infections depends mainly on humoral immune response. It starts as a local inflammation at the site of pathogen invasion. White blood cells arrive correlated with cytokines production. These events result to production of specific antibodies. Especially IgA; since sIgA have a major role in the body mucosal surfaces production against bacterial infections (Delves et al., 2006). The antibodies may be express in middle-ear fluids and serum early after infection (Howie et al., 1973; Kaur et al., 2012). Serum antibody plays an important role in middle-ear protection from bacterial infection. The infants are protected by passive antibody transferred from the mother (Salazar, 1997).

The middle ear is invaded by the upper respiratory commensals. The growth of the commensals in the middle ear frequently causes infectious events. Some of these infectious events occur in children repeatedly when the middle ear is in a state of immune tolerance, a condition in which T lymphocytes are unable to kill invading bacteria or viruses (Lin et al., 2014).

The major specific mediators of host defense in secretions are the immunoglobulins. IgG and IgA are the major immunoglobulins in secretions. IgG is a plasma protein that is distributed in the nasal mucosa by microvascular permeability and it is diffusing throughout the mucosa in highest concentration near the basement membrane. (Meredith et al., 1989)

2. Materials and Methods:

2.1 Sample collection:

One hundred blood samples were included in this study, all of them were adults, 40 chronic sinusitis patients and 40 of COM patients samples were collected. 20 blood samples were collected from healthy donors using as control group. Sera were separated using centrifuge (Hettich, Germany) at 3500 rpm at 10 minute and kept at -4°C until use.

2.2 Determination of immunoglobulins (IgA and IgG) levels:

the concentrations of IgA and IgG were estimated using single radial immunodiffusion technique for all samples included in this study.

2.3 Statistical analysis:

Independent T test was used to compare the differences between the concentrations means for patients and healthy donor sera using SPSS program. Results were considered significant at p(<0.05).
3. Results

3.1 Determination of IgG level

IgG level was measured in sinusitis patients and control group using single radial immune diffusion plate. Data analysis revealed that the concentrations mean of IgG in sinusitis patients (1078.6 mg/dl) was significantly (P < 0.05) lower than those of control group (1249.82 mg/dl), table (1). While the mean of IgG concentrations of otitis media patients (1338.77 mg/dl) was non significantly (P> 0.05) upper than those of control group(1249.82mg/dl),table(2).

Table (1): Serum IgG level in sinusitis patients and control group.

| Groups          | Range (mg/dl) | Mean (mg/dl) ± SD | P value |
|-----------------|---------------|-------------------|---------|
| Patients(40)    | 719.9-2107.5  | 1078.6 ± 270.0    | 0.000   |
| Control(20)     | 825.2-1564.6  | 1249.82 ± 354.48  |         |

Table (2): Serum IgG level in otitis media patients and control group.

| Groups          | Range (mg/dl) | Mean (mg/dl) ± SD | P value |
|-----------------|---------------|-------------------|---------|
| Patients(40)    | 719.9-2545.7  | 1338.77 ± 487.14  | 0.748   |
| Control(20)     | 825.2-1564.6  | 1249.82 ± 354.48  |         |

3.2 Determination of IgA level

Serum IgA level also measured by using IgA - single radial immune diffusion plate, statistical analysis for the results show no significant differences (P > 0.05) between IgA concentrations mean of sinusitis patients (244.4 mg/dl) and concentrations mean of control group (235.3 mg/dl),table (3). Significant differences (P<0.05) between IgA concentrations mean of otitis media patients (388.26mg/dl) and concentrations mean of control group (235.3mg/dl) were recorded ,table(4).

Table (3): Serum IgA level in sinusitis patients and control group.

| Groups          | Range (mg/dl) | Mean (mg/dl) ± SD | P value |
|-----------------|---------------|-------------------|---------|
| Patients(40)    | 114.1-308.8   | 244.4 ±83.8       | 0.834   |
| Control (20)    | 156.7-308.8   | 235.3 ±57.6       |         |

Table (4): Serum IgA level in otitis media patients and control group.

| Groups          | Range (mg/dl) | Mean (mg/dl) ± SD | P value |
|-----------------|---------------|-------------------|---------|
| Patients(40)    | 308.80-568.40 | 388.26 ±87.44     | 0.008   |
| Control(20)     | 156.7-308.80  | 235.3 ±57.6       |         |
4. Discussion

Chronic respiratory diseases including sinusitis, otitis media, and pneumonias have been associated with immunoglobulin deficiencies. (Hashemi and Madani , 2013). Bacterial sinusitis and otitis media are two of the most common indications for antimicrobial infections (Wald , 2011).

This study focused on the immunoglobulins (IgG and IgA) levels in two distinct clinical subgroups of URTI : sinusitis and otitis media. Sinusitis and otitis media samples were collected from different patients each patient suffering from one of included disease this enable us to determine the effect of each disease on immunoglobulins level.

Result of chronic sinusitis samples was appeared significant decreasing of patients IgG concentration comparing with control, this result indicated that there is an effect of IgG production in chronic sinusitis but the concentration remain within the normal value (800-1800 mg/dl) which recorded in leaflet of plate (Lta,Italy). Decreasing below the normal value may be recoded in IgG subclasses not in total IgG. Reductions in total IgG levels in adults or adolescents may be categorized as mild-moderate (300–600 mg/dl), significant (100–299 mg/dl) and profoundly reduced (<100 mg/dl). In adolescents and adults, humoral deficiency probably excludes when the summation of IgG ,IgM and IgA levels are greater than 600 mg/dl. (Sorensen and Moore, 2000).

IgG subclass deficiencies usually involve IgG2 or IgG3 with normal total IgG . IgM and other components of immune system remain within the normal values. IgG and its subclasses deficiencies have been distinguished as a critical factor for chronic sinusitis (Hashemi and Madani,2013) and Quinn and Ryan, (2002) reported the common immunodeficiency correlated with chronic sinusitis was a deficiency of IgG subclass.

A deficiency in IgG subclasses may not be determined by measuring total serum IgG because of very low concentrations of some subclasses. The concentration of IgG1, IgG2, IgG3 and IgG4 demonstrate 65%, 25%,7% and 3% of total serum IgG , respectively . Therefore the total IgG level remain within the normal value even their concentration is decreasing (Farhoudi et al., 1994; Pan and Hammarstrom, 2000)

Current result differed with Jiang and Hsu (2004) result , they found there were no significant differences in the levels of total serum immunoglobulins , also they found IgG subclasses levels recorded normal values in patients with chronic sinusitis .

Regarding the result of IgA concentrations, there was no significant differences between patients and control groups this result indicated that serum IgA concentration did not affect by this chronic disease. Because chronic sinusitis is one of the forms of mucosal inflammation, IgA in sinuses secretation may defect in the patients. Hsin et al.(2008) noted no differences in the levels of total and secretory IgA among the chronic sinusitis patients. Also Hashemi et al. (2012) indicated that chronic inflammation in sinuses did not influence the lacrimal IgA level when compared with normal control. Secretory IgA level of nasal secretion was elevated in patient with chronic sinusitis patients (Mogi and Kurono,1987). Carenfelt et al. (2009) study referred to significant decreasing in IgA level in purulent sinus secretation comparing with serous secretation. Hamaguchi et al. (1981) referred to the immunoglobulins levels were different between purulent and mucus secretion of sinus with chronic inflammation and the local synthesis of IgG and IgA were active in nasal mucosa. Low level of IgG and IgA subclasses were common in chronic or recurrent sinusitis patients (Seppänen et al., 2006).

OM was the other URTI disease which selected to include in present study for comparing between the effect of the two diseases on serum immunoglobulins levels. The result revealed that IgG concentration recorded no significant difference between patients and control sera whereas IgA concentration in otitis media patients significantly elevated upon control group. Serum antibodies have a significant role in middle ear protection from bacterial infections (Kaut et al., 2012). Immune response against infections of otitis media depends mainly on humoral mediated immune response. It starts as local inflammation at the pathogen invasion site . These events end with specific antibodies production especially IgA (Delves et al., 2006).

Freijd et al.(1985) and Sorensen and Nielsen (1988) reported lower levels of IgG2 in children with recurrent otitis media compared with controls .The resultant of Al-Hamadany, (2017) study revealed suppurative otitis media caused significant elevations in total white blood cells count. Immunoglobulins
(IgM, IgG and IgA) and the complement components when estimated by single radial immunodiffusion whereas present study recorded normal level of level of IgG and elevated level of IgA.

Veenhoven et al. (2004) concluded that high percentage of low IgG2 levels was recorded in children with recurrent otitis media. Otitis prone children in general showed lower total IgA, IgM, IgG, IgG1, and IgG2 levels compared with children with fewer episodes while Berman (1992) referred to children with recurrent acute otitis media were found to have increased or infections serum IgM, IgA, IgG, and IgG1 levels compared with normal values for age, whereas serum IgG2 values were mostly in the lower normal level. Twenty-two percent of children showed IgG2 values lower than the age-specific mean.

Krakau et al. (2014) recorded a cases of recurrent otitis media with low IgG2 level during childhood but normal immunoglobulins pattern in adulthood. The antibody detected in the middle ear of children derives from transudation of serum and IgA reflux from the nasopharyngeal (Kaur et al., 2012).

The concentration of IgA was greater in middle ear fluid than in serum almost half the patients, and the mean middle ear fluid to serum ratio for IgA was 1.38. Thus, it would appear that in this disorder middle ear fluid represents primarily a secretory response to inflammation rather than a transudate. (Howie et al., 1973)

This study concluded that chronic sinusitis cause decreased of IgG while COM cause increased IgA level. In general the immunoglobulins concentrations were mild moderate.

5. References

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