

## Prevalence and pathogenesis of otosclerosis: A review

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### ABSTRACT

The current review is aimed to provide an overview of etio-pathogenesis of otosclerosis. Otosclerosis affects bony labyrinth resulting a progressive conductive hearing loss, a sensorineural hearing loss, or a mixed-type hearing loss. It is a hereditary localized disease of the otic capsule typified by new bone formation that is composed of different fibrillar and cellular pattern. The abnormal new bone produces ankylosis of the stapes footplate resulting in conductive deafness. The onset of the hearing loss due to otosclerosis is usually between 15 and 40 years of age. Otosclerosis is a disease of adult onset affecting more women than men in the world. The previous study also has identified the link of otosclerosis with the family history. Additionally, women at an earlier age reported greater severity of otosclerosis symptoms compared to men. Despite the numerous theories suggested, the etiology of otosclerosis has remained obscure. Since histopathological inner ear changes due to otosclerosis is important, this review will provide an updated overview of prevalence and etio-pathological changes in otosclerosis.

**KEY WORDS:** OTOSCLEROSIS, HEARING LOSS, OTOSPONGIOSIS, COCHLEAR LESIONS

### INTRODUCTION

Otosclerosis is a disease of the bony labyrinth, which is characterized by fixation of the footplate of the stapes secondary to abnormal bone formation (Quesnel et al., 2018; Guild, 1994; Schuknecht, 1993). The area of the labyrinthine capsule immediately in front of the footplate of the stapes called “fissula antefenestrum” is

the site of predilection for otosclerosis. Other frequent sites include the border of the round window and even the footplate of the stapes (Mansour et al., 2018; Guild, 1994; Schuknecht, 1993).

Virolainen (1972) reports that otosclerosis is usually bilateral. It is a hereditary localized disease of the otic capsule typified by new bone formation that is composed of different fibrillar and cellular pattern (Sho-

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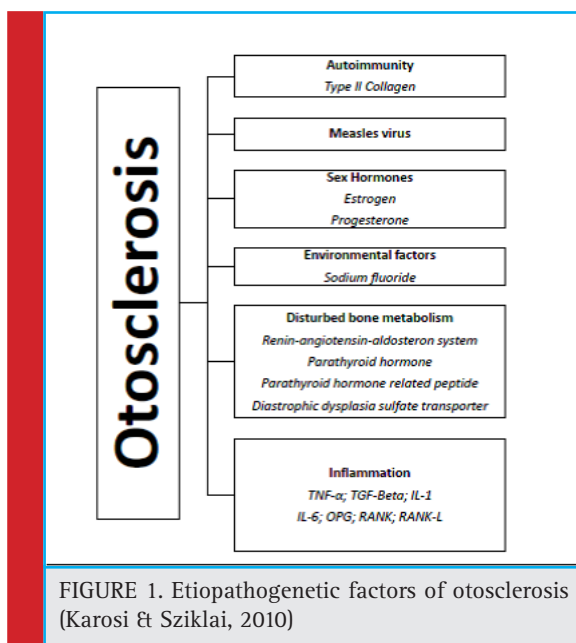
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man et al., 2014; Guild, 1994; Schuknecht, 1993). The abnormal new bone produces ankylosis of the stapes footplate resulting in conductive deafness (Henriques et al., 2016; Guild, 1994; Schuknecht, 1993). Other part of the labyrinth may be involved resulting in sensorineural deafness and vestibular abnormalities (Ciuman, 2013; Smyth, 1997).

“Otospongiosis” is the other term for this condition and is preferred by many European otologists, as the abnormal new bone is highly vascular (Bittermann, 2014; Causse and colleague, 1984). However, in UK, the term “otosclerosis” is commonly used, which refers to the final inactive stage where there is sclerotic hard bone (Virolainen, 1972). According to Smyth (1997) neither of these terms is strictly correct.

Despite the numerous theories suggested, the etiology of otosclerosis has remained obscure. Delayed physiological development, inflammatory processes, cartilaginous deposits in the region of the fissa antefenestrum, disturbances in the blood supply, mechanical stimuli, etc. have all been described as possible cause of otosclerosis (Batson and Rizzolo, 2017; Cureoglu et al., 2006) (Figure 1). It is therefore possible that there are constitutional, local and activating factors, which could be responsible for the development of the otosclerotic foci either individually or jointly (Virolainen, 1972). This review aimed to provide an overview of prevalence and etio-pathogenesis of otosclerosis.



## REVIEW OF LITERATURE ON OTOSCLEROSIS

In the past years the study of otosclerosis has principally been devoted to the histochemistry of otosclerotic foci (Abdel-Ghany et al., 2014). A significant elevation in the

activity of alkaline phosphatase and an equally significant fall in the activity of lactic acid dehydrogenase has been described (Moumoulidis et al., 2007). Some changes in the matrix of the otosclerotic bone have also been shown, for instance in the number and construction of the polysaccharides (Virolainen, 1972; Ziff, 2014).

Otosclerosis is a disease of adult onset affecting more women than men in the world (Crompton et al., 2019). The previous study also has identified the link of otosclerosis with the family history (Crompton et al., 2019). Additionally, women at an earlier age reported greater severity of otosclerosis symptoms compared to men (Crompton et al., 2019). Clinical manifestation of otosclerosis is more evident in White Europeans and people of Indian origin (Lin et al., 2007).

In addition to typical conductive hearing loss, patients suffering from otosclerosis also often have perceptive hearing loss (Cureoglu et al., 2010; Venail et al., 2007). Cochlear lesions are considered to be due to secretions from the active otosclerotic foci, which have found their way into the endolymph (Makarem and Linthicum, 2008). Vestibular disturbances even appear in patients suffering from otosclerosis (de Vilhena et al., 2016). These may be derived from otosclerotic vascular changes due to the disease or from biochemical changes in the inner ear fluids (Ciuman, 2013).

Because hearing loss is the dominant feature of otosclerosis, these patients have not been examined for the other disorders associated with otosclerosis as carefully as for hearing (Declau et al., 2007). Unsteadiness and or dizziness have been frequently observed in these patients (Yetişer, 2018). Abnormal electronystagmographic findings have been reported in otosclerotics (Gupta and Mundra, 2015). Further studies of these changes would throw additional light on the general view about otosclerosis (Purohit, 2014).

## OCCURRENCE OF OTOSCLEROTIC FOCI

It's important to distinguish between clinical, non-clinical or histological otosclerosis; the latter is about 10 times more common than the former (Smyth, 1997; McElveen and Kutz, 2018). In 1940, first study revealed histological otosclerosis on the temporal bones in 12% of 200 autopsies (Virolainen, 1972). In 1944, Guild demonstrated histological otosclerosis in only 8.3% of 482 African races but much less in the wider population around 1%. A recent histological study reported lack of evidence for nonotosclerotic stapes fixation in people undergoing stapedectomy (Quesnel et al., 2016).

Otosclerosis is usually bilateral, however the frequency of histological unilateral otosclerosis ranges between 13% and 30% (Foster and Backous, 2018; Quesnel et al., 2018). The area of the labyrinthine capsule immediately

in front of the footplate of the stapes called 'fissula antefenestrum' is the site of predilection for otosclerosis; other frequent sites may include border of the round window and even the footplate of the stapes around the cochlea, the internal auditory canal or less often around the semi-circular canal (Michaels and Soucek, 2011).

The focus nearly always originates in the endochondral layer of the labyrinthine capsule, extending in many cases into the periosteal layer as far as the mucosa of the tympanic cavity, and into the endosteal layer of the labyrinth (Naumann et al., 2005). Where the focus reaches the mucoperiosteum of the tympanum and the endosteum of the labyrinth, these show varying degrees of fibrous thickening and increased vascularity (Makarem et al., 2010).

Virolainen (1972) quotes Seligman and Shambaugh (1951) that assessment of 2086 post-operative surgery of ear revealed that cochlear nerve involvement is present twice as often when otosclerotic foci are situated in the horizontal semicircular canal, compared with the frequency of the involvement when the canal is not affected. Histological otosclerosis is at any rate quite frequently asymptomatic (Declau et al., 2007). In a previous review of Ménière's disease, the lateral semicircular canal was found at autopsy to be full of otosclerotic bone (Oberman et al., 2017).

## PATHOLOGICAL CHANGES IN OTOSCLEROSIS

Otosclerosis is a disease of the bony labyrinthine capsule, frequently developing in areas where embryonic cartilage persists (Bloch, 2012; Babcock et al., 2018). The pathological process is characterized by resorption of the normal bone, often around the blood vessels, and by the replacement of normal bone with cellular fibrous connective tissue (Rudic et al., 2015). Areas undergoing active resorption are extensively vascularised (Rudic et al., 2015). Focus may contain areas at different stages of activity that can be described as active intermediate and inactive final stage (Karosi & Sziklai, 2010). Karosi et al., (2011) reported that the activity of alkaline phosphatase increases in the focus.

The term "otospongiosis" refers to the active phase of the disease, which is characterized by the presence of vascular space containing highly cellular fibrous tissue, mononuclear histiocytes together with osteocytes and osteoclasts (Parahy and Linthicum, 1984; Uppal et al., 2010). These cells contain many enzymes, which are released in to the surrounding tissues resulting in its absorption (Ziff, 2014). The term "otosclerosis" refers to the final stage of highly mineralized bone with a mosaic appearance (Quesnel et al., 2013). Osteoclasts have disappeared but osteocytes and/or osteoblasts may still be seen in the peripheral areas (Quesnel et al., 2013).

Previous study had suggested that some enzyme serve as the initiating factor of decalcification (Purohit & Hermans, 2014). Another study suggested that the focus shows alkaline phosphates during the first phase and the whole of secondary phase until the bone is completely calcified, alkaline phosphatase will then disappear (Gronowicz et al., 2014). Some studies observed the presence of abnormal accumulation of mucopolysaccharides in to the otosclerosis focus (Ricci, 1962; Ribári et al., 1991). A recent study reported higher level of total oxidant status and oxidative stress index in patients with otosclerosis (Baysal et al., 2017). Additionally, reactive oxygen species could be developed in otosclerotic foci (Rudic et al., 2015).

## PERILYMPH CHANGES IN OTOSCLEROSIS

The perilymph has an extra-cellular character with low potassium, glucose, amino acid, and high sodium concentration (Palmer et al., 2016). The blood-labyrinthine barrier permeability has been slightly increased in ears of patients with Ménière's disease (Tagaya et al., 2011). Additionally, the blood-labyrinthine barrier permeability is also increased in other diseases, for instance sudden deafness (Sugiura et al., 2006; Yoshida et al., 2008), labyrinthine invasion of cholesteatoma (Sone et al., 2007; Sone et al., 2012), vestibular schwannoma (Yamazaki et al., 2009), and relapsing polychondritis (Kato et al., 2014). Endolymphatic hydrops (EHs) is often seen in patients with otosclerosis, and preoperative EH was one of the risk factor for inner ear disturbances following stapes surgery (Mukaida et al., 2015). Furthermore, increased permeability of the blood-labyrinthine barrier and endolymphatic hydrops could also causes sensorineural hearing loss in otosclerosis (Mukaida et al., 2015). A recent study assessed and compared cochlear lymph signal intensity in patients with otosclerosis, Ménière's disease, and healthy individuals (Naganawa et al., 2016). The results of this study indicated an increased cochlear lymph signal intensity ratio in patients with otosclerosis than Ménière's disease or healthy individuals (Naganawa et al., 2016). Many studies has been reported an association of EH with otosclerosis (Franklin et al., 1990; Yoon et al., 1990; Shea et al., 1994); however, there is a lack of understanding about the mechanism for the development of EH in patients with otosclerosis (Mukaida et al., 2015).

## CONCLUSIONS

The histological and pathological changes of otosclerosis is still not fully explained. To enhance a better understanding of the pathogenesis of otosclerosis, it is vital to use modern biologic methods to examine pathological changes in human temporal bones with otosclerosis.

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