The Egyptian Journal of Hospital Medicine (October 2017) Vol.69(1), Page 1698-1705

Review of Microtia: A Focus on Current Surgical Approaches

Nujaim H. Alnujaim[1], Mohammed H. Alnujaim[2]
[1]Division of Plastic and reconstructive surgery, Department of Surgery,
King Saud University, Riyadh, Saudi Arabia
[2]College of Medicine, King Saud University, Riyadh, Saudi Arabia
Corresponding author: Dr. Nujaim Hamad Alnujaim, Tel: +966506688244, Email: Nujaimhs@gmail.com

ABSTRACT

A wide spectrum of anomalies may involve the auditory system. As a visible structure, auricular malformations constitute a great burden. A wide set of anomalies may affect the ear including the microtia spectrum, protruding ears (bat ear), constricted ear (Lop and Cup ears), Stahl ear, and cryptotia. In plastic surgery practice protruding ears and microtia are common presentations. Microtia literally means *small ears*. Microtia is a spectrum of anomalies of the auricle that range from disorganized remnant of cartilage attached to soft tissue lobule to complete absence of the ear (anotia). Ear reconstructive procedures has made in impact in the lives of these patients. The early attempts to surgically restore the ear in microtia was in ***1920*** using a rib cartilage**.** Up to 49% of microtia cases are associated with other anomalies or a known syndrome. The most common syndromic associations are *hemifacial microsomia, Towens Brocks syndrome, Treacher Collins, Goldenhar and Nager syndrome.* O*culo-auriculo-vertebral spectrum (OAVS).* Generally, the ear can be retrieved by two possible methods: *Surgical reconstruction* using *autologous* or *alloplastic* cartilage and the use of *prosthesis* which could be adhesive or implant retained. Surgical reconstruction proved to be superior to other methods due to its longevity and less complications. The only limitation is the skill of the surgeon. Ear prosthesis are reserved for special cases including traumatic anotia in adults.

Keywords: Microtia, Reconstruction, Malformation, Nagata, Brent.

INTRODUCTION

Congenital deformities may involve any part of the body, of which those involving the craniofacial skeleton constitute a much greater burden. A study by ***Weerda et al.*** [1]states that the ear is more likely to be congenitally malformed compared to the nose and throat due to the complex embryology of the ear. Ear malformation may involve the outer auricle, external auditory canal, middle and inner ear. Most of outer and middle ear malformations are right sided and unilateral, while inner ear malformations can be unilateral or bilateral [1, 2, 3] . Different parts of the human ear develop separately as such a combination of outer, middle and inner ear deformities are quite rare. A combined ear deformity described by ***Swartz and Fearber et al.*** [2] known as ***atresia auris congenita*** where the outer and middle ears are malformed and occasionally the inner ear. A wide spectrum of anomalies may involve the auditory system. The auricle may be malformed in terms of orientation, size and position. The external auditory canal can be aplastic or hypoplastic. The middle ear structures including the ossicles, round and less likely the oval window can be malformed. Congenital ossicular malformation are described to affect the size, number and configuration of the ossicles. In addition, middle ear space and configuration are occasionally malformed [4]. Minor Middle ear anomalies are exclusive to the middle ear and do not involve the tympanic membrane or the external ear and are classified by ***Teunissen and Cremers*** in 1993 based on surgical approach into ***four*** main groups: ***isolated stapes ankylosis, stapes ankylosis associated with other ossicular malformations, deformity of the ossicular chain with mobile stapes footplate, and severe aplasia or dysplasia of oval or round windows*** [5]. Inner ear malformations are either due to arrested or abnormal development and include ***Michel deformity (Labyrinthine aplasia), cochlear aplasia/hypoplasia, common cavity, incomplete partition, and large vestibular aqueduct (LVA) syndrome*** [6] .

Despite the morbidity associated with middle and inner ear congenital anomalies in terms of effect on hearing, the auricle a visible part of the auditory system contributes significantly to facial beauty. Therefore, a normal structure and position of the auricle is preferred to maintain a desirable appearance. Various congenital malformation may affect the auricle and cause a long-lasting

Received:1 /7 /2017
Accepted: 10/7 /2017
DOI : 10.12816/0040136

psychological distress and include ***the microtia spectrum, protruding ears (bat ear), constricted ear (Lop and Cup ears), Stahl ear, and cryptotia***. In plastic surgery practice protruding ears and microtia are common presentations. A study done by ***Litschel R et al.*** [7] to quantify the attention to individuals with protruding ears and its effect on personality. The study concluded that protruding ears draw the attention of public, but they do not have a negative impact on personality perception. Another study by ***Byun et al.*** [8] to evaluate public perception of microtia found that microtia comparable to monocular blindness among other less stigmatizing conditions, as such it is viewed in the eyes of public as a handicap.

Microtia literally means *small ears*. Microtia includes a spectrum of anomalies of the auricle that range in severity from disorganized remnant of cartilage attached to soft tissue lobule to complete absence of the ear (anotia) [9].A review of literature revealed no consensus on the naming, some authors use the term *microtia* to indicate the full spectrum of the anomaly while others simply refer to it as *microtia/anotia* spectrum [10, 11, 12]. Interestingly, ear tags are also regarded as part of microtia/anotia [9] . Mostly, it is a unilateral anomaly with a right side dominance [13]. While Microtia is typically an external ear deformity, these patients suffer from *conductive hearing loss* due meatal, external auditory canal or tympanic membrane abnormalities [9]. As a birth defect, microtia can be an isolated anomaly or part of a syndrome. Bilateral microtia is more likely to be syndromic [14] . As a visible deformity, patients usually have psychological issues. Ear reconstruction has alleviated the high rates of anxiety and depression suffered by these patients with a much-improved social interaction [15].

Reconstruction of the ear is recognized as a demanding procedure with unfavorable outcomes even in the hands of expert surgeons. The limitations of the surgery are usually due to the underlying tissue shortages, a limited donor tissues, and some are due to the surgeon himself. Even more demanding is the revision surgery for a previous unsatisfactory result, with a scarred recipient and even more limited donor site. As such, ear reconstructive surgery for microtia is a challenge to every plastic surgeon, with a continuous research to develop more effective techniques to counteract all the possible limitations. *Our aim from this article is to review the most recent ligature in microtia with a special focus on surgical reconstruction.*

MICROTIA SURGICAL REPAIR THROUGH HISTORY

The early attempts to surgically restore the ear in microtia was in ***1920*** using a rib cartilage by **Gillis**. Soon after, several reports emerged regarding the use of allogenic cartilage as possible substitute, but unfortunately most of these attempts failed as the allogenic cartilage was reported to be slowly resorbed [16]. **Tanzer** [16] established the modern era of auricular reconstruction by the reintroduction of autogenous cartilage graft. The promising results of **Tanzer** inspired **Brent** who modified the techniques of Tanzer and created *the four-stage repair of microtia*. Later, **Nagata** [17] created a more complex technique for auricular reconstruction with only *two stages of repair*. Despite the less stages, Nagata created a more detailed ear framework than **Brent** [18] at the expense of using more cartilage.

Recently**,** *artificial materials* have been explored as a mean to spare the rib cartilage. ***Silastic***, an artificial substitute is used for auricular reconstruction, but this and other artificial materials have been associated with a higher rate of extrusion. ***Porous Polyethylene*** has been explored as possibility for ear reconstruction and is now considered a standard of care by many surgeons[19]. Finally, ***auricular prosthesis*** has indeed stabilized auricular reconstruction and made it possible for many surgeons to operate safely.

EPIDEMIOLOGY

External ear anomalies are common in up to 5 % of the population [20] . ***Forrester et al .***[23] study reports the prevalence of microtia in the United States to be ***2 – 3/10000 births,*** with a greater increase in Hispanics and Japanese. ***Shaw et al.*** [22] determined the prevalence of microtia through a population based registry where the data is derived from the California Birth Defects Monitoring Program with 2.5 million birth and stillbirths from the period of 1989 - 1997. The prevalence was ***2.50 /10,000*** live births and stillbirths. Syndromic microtia was reported to be higher than isolated microtia with **1.53/10000** births compared to **0.63/10000** births. It was also found that Hispanics and Asians are more likely to have microtia/anotia compared to Caucasians. ***Canfield et al.*** [12] obtained

data from Texas Birth Defects Registry and determined a prevalence of ***2.86/10000*** live birth along with increased incidence among Hispanics and a higher maternal age. A study in china revealed a prevalence of microtia to be **1.4/10000** births [24]. Males were also found to be more predisposed to microtia/anotia [23, 24]. An interesting finding by ***Castilla et al.*** [25] which reported a higher prevalence of microtia along with other craniofacial anomalies in higher altitudes in Latin America. At an altitude above 3000ft in the Ecuador a microtia prevalence of **17.4/10000** births was reported. Moreover, a recent study in 2016 by ***stoll et al.*** [33] in France established the prevalence of anotia microtia on 387067 births with a ratio of 3.77/10000 births.

RELEVANT ANATOMY AND EMBRYOLOGY

The ear is made of a complex-shaped cartilage covered on its visible surface with thin, tightly adherent skin. A consideration must be made when reconstructing an ear to be more rigid than the normally delicate ear. A reconstructed ear reaches its final shape through a series of scar contracture, which would eventually accentuate the fine sculptures made by the surgeon. As such, imperfect results are expected even when using the best techniques for auricular reconstruction. While the current techniques have their own deficiencies, the surgeon should pay more attention to the size, position and proper angulation of the ears relative to other structures.
Most patients with microtia have atretic auricle, external auditory canal and tympanic membrane with variable involvement of the ossicles. The middle and external ears are derivatives of the first and second branchial arches. The auricle is made from several bulges in the first and second arches known as auricular hillocks. Each of the hillocks contributes to a specific part of the pinna, and those in the second arch form most of the auricle. Hillock development usually occurs slowly over a period of months, with the overlying ectoderm having a significant role in the final form of the auricle. The inner ear on the other hand have a completely different embryological origin, therefore it is always normal in patients with microtia/anotia [26].

RISK FACTORS AND ASSOCIATED ANOMALIES

Several case control studies and population based cross sectional studies extensively investigated the possible risk factors associated with microtia/anotia. The risk factors reviewed are generally either due to maternal illness or exposure to certain medications during pregnancy. High maternal or paternal age, multiple births, and maternal type 1 diabetes are well documented risk factors [22-25].A Japanese study by ***Okami et al.*** [34] on 592 patients with microtia showed a significant association between microtia and gestosis, maternal cold , spontaneous abortion, and anemia. Several epidemiological studies have linked *Hispanic* race and high altitude to the occurrence of anotia/microtia [22-26]. Low birth weight is also associated with microtia, but no causal relation is found between the two [27]. Retinoids, thalidomide and mycophenolate mofetil are strongly associated with microtia/anotia [35,36].

The most recent literature by ***Stoll et al.*** [33] who stated that up to 49% of microtia cases are associated with other anomalies or a known syndrome. Although, the percentage has varied widely in previous literature ranging between 20 - 60% [22,25,28,14]. Non syndromic congenital malformations involving the heart, kidney and the facial skeleton including facial clefting, and asymmetry are also reported with a varying percentage [9,24.27] . Several other studies demonstrated the association of microtia with chromosomal aberrations including 13, 18, and 21 with a percentage ranging from 2% to 14% [22,14] . The association with chromosome 18 is the most common according to ***stoll et al.*** [33] recent study which is consistent with other literature. These findings nescciates the examiner to look for the other possible syndromes, to provide the optimal treatment.

The most common syndromic associations are *hemifacial microsomia, Towens Brocks syndrome, Treacher Collins, Goldenhar and Nager syndrome.* O*culo-auriculo-vertebral spectrum* ***(OAVS)***, is characterized by microtia, ear tags, epibulbar dermoids, microphthalmia, and macrostomia [14]. OAVS and microtia/Anotia spectrum share many similarities in terms of mode of inheritance, right side and male dominance. Therefore, some authors regard them as one anomaly with two extremes of severity[27] .

CLASSIFICATION OF MICROTIA

A complex malformation such as microtia requires a standardized classification to facilitate further understanding. A Review of literature revealed several classifications for microtia

beginning with ***Marx classification***[28] *in* ***1926*** and ending with ***hunter et al.***[29] classification in **2009**. Most relied on the surgical approach, and some on morphology and embryological development for classification. ***Weerda classification***[30] is now the standard for describing microtia. A summary of the classifications published in literature is presented in **Table 1. Figures 1 – 4** show the different grades of microtia according to ***Marx classification.***

Marx (1926)[28]
Grade I: a normally structured auricle, but smaller than normal
Grade II: Abnormal auricle with some identifiable features
Grade III: Rudimentary ear
Grade IV (added from Rogers 1977): Anotia
Tanzer (1978)[31]
Type 1: Anotia
Type 2: Completely hypoplastic ear (microtia)
a. With atresia of the EAC b. Without atresia of the EAC
Type 3: Hypoplasia of the middle third of the auricle
Type 4. Hypoplasia of the superior third of the auricle.
a. Constricted (cup and lop) ear. b. Cryptoptia. c. Hypoplasia of entire superior third.
Type 5. Prominent ear
Weerda (1988)[30]
First degree Malformation: Most structures of a normal auricle are recognizable (minor deformities).
a. Macrotia b. deformities of tragus and antitragus c. Protruding ears d. Colobomata e. Cryptoptia f. Lobule deformities g. Absence of upper helix h. Cup ear deformities i. Stahl ear
Second degree Malformation: Some structures of a normal auricle are recognizable. eg.mini ear
Third degree Malformation: None of the structures of a normal auricle are recognizable. Classified as unilateral or bilateral. Anotia is included in this category
Nagata (2000)[32]
Lobule-type: Remnant of the auricle and lobule; without the concha, EAC, and tragus
Concha-type: Variable degree of presence of the lobule, concha, EAC, tragus, incisura tragica
Small concha-type: Remnant of the auricle and lobule with a small indentation representing the concha
Anotia: None or only minute resemblance of a remnant auricle
Atypical: Cases that do not fall into any of the above classifications
Hunter et al, (2009)[29]
Microtia, First Degree. Presence of all the normal ear components and the median longitudinal length more than 2 SD below the mean.
Microtia, Second Degree. Median longitudinal length of the ear more than 2 SD below the mean in the presence of some, but not all, parts of the normal ear.
Microtia, Third Degree. Presence of some auricular structures, but none of these structures conforms to recognized ear components
Anotia. Complete absence of the ear

Table 1. Classification of microtia

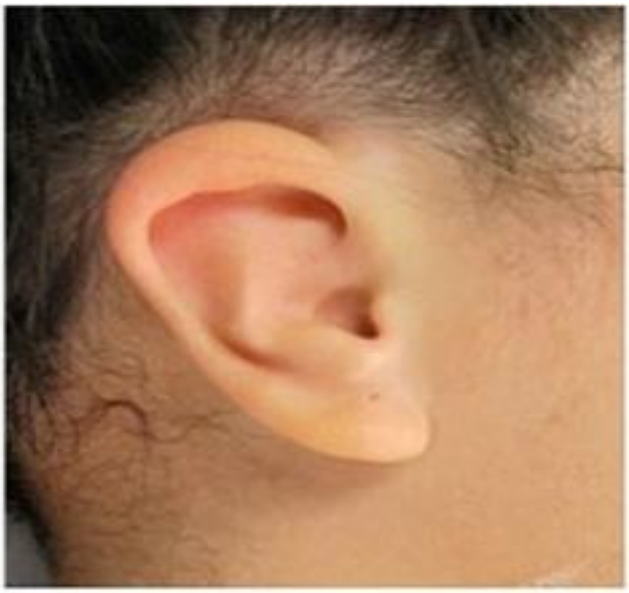

Figure1. Grade 1 Microtia

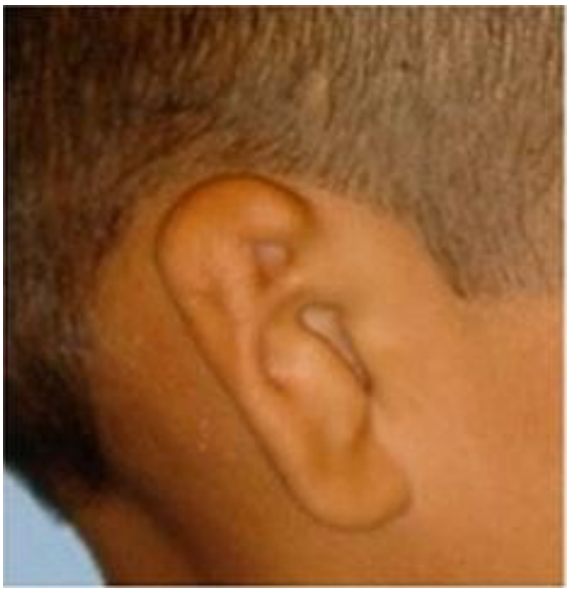

Figure 2. Grade 2 Microtia

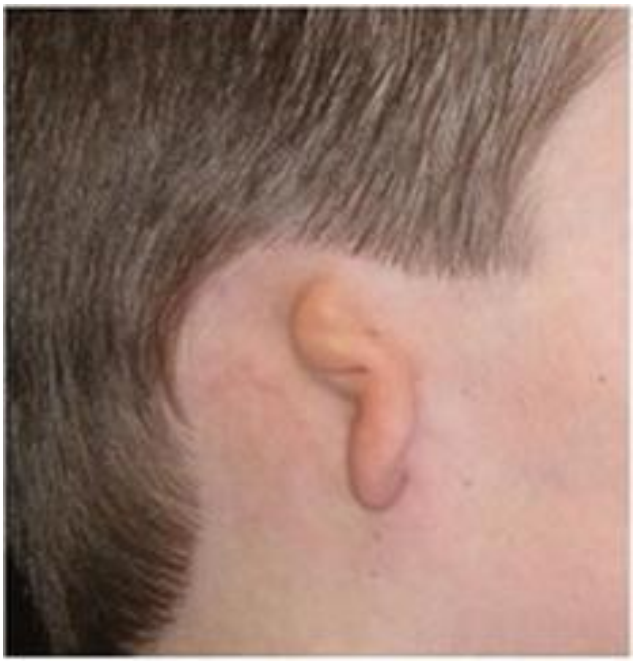

Figure 3. Grade 3 microtia

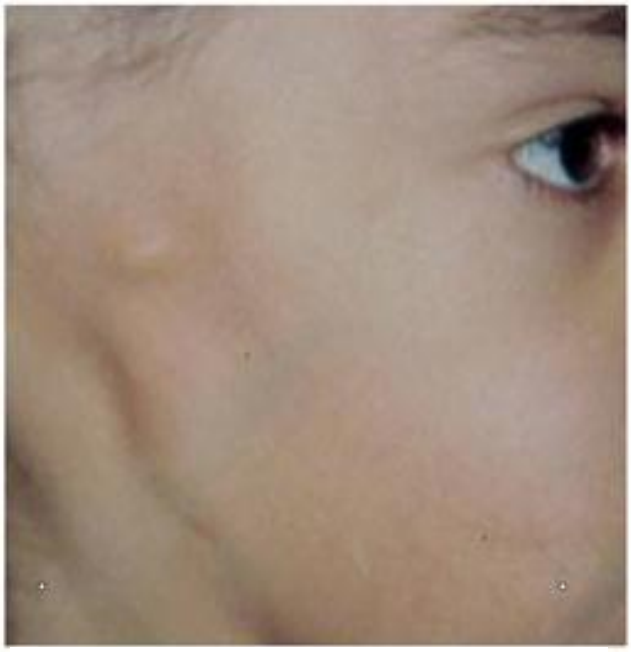

Figure 4. Grade 4 microtia (anotia)

All the pictures in this review are adapted with permission from http://craniofacialteamtexas.com/

MANAGEMENT

Reasonable goals in reconstruction of microtia are a satisfied patient, proper position, adequate size and contour. It must be explained to the parents that a reconstructed ear is in elastic and will not duplicate the original ears. Even when effort is made to ensure a detailed ear framework, several minor complications may occur and negate the efforts. These include poor healing, infections, hematoma or skin break down. By age 7, the ears have achieved much of their adult size. As the child grows, the thoracic cavity increases in size such that by age 6 adequate donor cartilage may be available as such patient is ready for surgery. As the child grows, more cartilage becomes available, making

reconstruction easier. However, waiting for maturity of donor cartilage must be weighed against the child psychological status [40].

Generally, the ear can be retrieved by two possible methods:

1. *Surgical reconstruction* using *autologous* or *alloplastic* cartilage.
2. The use of *prosthesis* which could be adhesive or implant retained.

Autologous Ear reconstruction

We describe in this part the works of Brent and Nagata in ear reconstruction. Brent created the classic four staged repair operations for microtia and was modified by Nagata into a 2-staged operation. Brent procedure was more suitable to the *lobule type microtia* as the second stage involves the transposition of the already existing lobule, but at the expense of keeping the patient a longer time. On the other hand, Nagata surgery was better suited for the conchal bowel type microtia with a 1 cm vascularized pedicle serving as the new ear lobule created at the same time as the new ear framework in a single stage. *The following is the summary of Brent four stages procedure and Nagata two stages procedure:*

Brent Surgical Technique [18,40]

Stage 1: Ear framework reconstruction

Preoperatively, three templates using radiograph film is made. The first will show the helical rim tragus, antitragus and conchal bowel. The second template will outline the same landmarks above without the helical rim which will be used to harvest the base of the framework from the sixth and seventh ribs before the helical rim is added. A Third template with markings toward the lateral canthus and oral commissures are made to ensure proper positioning on the opposite side of the normal ear. Additionally, the distance from the lateral canthus to the helical root should be measured to confirm correct distances as marked on the template. The surgery is performed under general anesthesia with face and both ears fully exposed. The contralateral cartilaginous portion of the sixth to eighth ribs is harvested since the curvature of the thorax can be used to our advantage. Dissection then begins at the inferior margin of the costal cartilage. Lateral dissection is then performed to identify the eighth rib. Ribs are dissected posterior to the Osseo cutaneous junction. The ribs must not be cut until they have been exposed to the Osseo-chondral junction. The second template is placed over the cartilaginous joint of the rib between the sixth and seventh ribs. It must be ensured that the cartilage is cut with the entire perichondrium intact as well as the entire cartilaginous portion of the eighth rib. After that an incision is made over the microtic ear to remove the remnants.

The base of the framework is made from the sixth and seventh ribs. The helix is reconstructed from the eighth rib, which is made thinner to allow it to bend. The two parts are then joined together. The framework is then inserted into the previously dissected remnant in an upside-down manner and with rotation into correct position. After that a dressing is put for 3 days.

Stage II: Lobular transposition

Under local anesthesia in an outpatient basis. This is done 6 to 8 weeks after the first stage of reconstruction. This stage is assuming the presence of a remnant lobule which usually place superiorly than normal. The remnant is made into a pedicled flap and is rotated inferiorly. An inferior incision is made over the helix to allow positioning of the new lobule.

Stage III: Frame Elevation

Performed under general anesthesia. The framework is freed from the underlying soft tissue. The scalp posterior to the incision is dissected extensively, an advancement flap is created to cover the new postauricular sulcus and now remains the posterior surface of the framework. A split thickness skin graft from the buttocks or a full thickness skin graft from below the umbilicus is made to cover the posterior defect.

Stage IV: Tragus Reconstruction

A composite graft from the opposite conchal cartilage is used to reconstruct the tragus and then the donor site can be closed primarily

Nagata surgical technique [17,41]

Stage 1

The procedure is done under general anesthesia. In Nagata technique, framework and tragus reconstruction in addition to lobular transposition are done in stage 1.

Stage II

The procedure is done as an outpatient. The framework is freed, and the ear is elevated. Cartilage harvested from the first stage is usually stored beneath the skin is now retrieved and cut to create a wedge. This is placed posterior to the elevated ear and covered with a flap. An advancement flap is made to cover the mastoid cortex. A skin graft is made to cover the posterior defect of the ear.

Alloplastic Ear Reconstruction

The auricular framework composed of ***porous polyethylene (Medpor)*** is used instead of costal cartilage. The addition of temporoparietal flap to cover the frame decreased the complication of implant exposure. This type of reconstruction has the advantage of being a single stage procedure. An incision is made

posterior to planned position of alloplastic implant. The cartilage is removed and skin is thinned. For dissecting TPF (temporoparietal) flap the superficial temporal artery pedicle is identified and preserved. The high-density porous polyethylene implant is collected and joined together using a cautery that melts the pieces together. The flap then covers the implant. A skin graft is then applied over the flap. A dressing is applied [42].

Complications

For cartilage reconstruction, the most common complications are exposure due to a local infection, malposition, low-lying hair, resorption, delayed fracture, and disarticulation. Alloplastic reconstruction is reported to have less complications compared to cartilage reconstruction[43].

Prosthetic ear replacements

An ear prosthesis can be retained to the skull by either adhesives or an implant, adhesives were an impractical method. Osseo integrated titanium implants made prosthetic replacements more practical by placing a titanium anchored to the temporal bone. Prosthesis are Usually not the best method for children as they refuse to wear them[44]. They are more liable to infections which will necessitate their removal until the infection is dealt with. Moreover, the removal of these prosthesis will serve as a reminder to these children that they are still having a malformed ear. Ear prosthesis for children usually have an integrated hearing aids and must be replaced every 5 years, which would be expensive[44]. Probably the absolute indications for prosthesis are a failed autologous reconstruction for a child or a traumatic anotia in an adult [40]

CONCLUSION

In conclusion, microtia constitute a heterogenous group of malformations occurring at rate that should draw the attention of every plastic surgeon, otorhinolaryngologist and the general medical field. Reconstruction of the ear is as stated a challenge to every surgeon, but at the same time probably one of the most rewarding surgeries. The continuing research in stem cell will open the doors for the creation of replacement tissue without sacrificing the existing donor tissue and will enable more surgeons to operate confidently and with improved results.

REFERENCES

1. **Weerda H (2004):** Chirurgie der Ohrmuschel. Verletzungen, Defekte und Anomalien Stuttgart, Thieme, S. 105-226.
2. **Swartz JD, Faerber EN (1985):** Congenital malformations of the external and middle ear: high-resolution CT findings of surgical import. AJR.,144:501-6.
3. **Thorn L, Entwicklung d (1994)**: Einschließlich Entstehung von Missbildungen, experimentelle Embryologie und In-vitro-Studien. In: Helms J, Hrsg. Oto-Rhino-Laryngologie in Klinik und Praxis. Bd. 1. Stuttgart: Thieme, S. 1-22
4. **Marangos N (2002):** Dysplasien des Innenohres und inneren Gehörganges. HNO.,50(9):866-81
5. **Teunissen E and Cremers W (1993):** Classification of Congenital Middle Ear Anomalies Report on 144 Ears. Annals of Otology, Rhinology & Laryngology, 102(8):606-612.
6. **Sennaroglu L (2010):** Cochlear Implantation in Inner Ear Malformations — A Review Article. Cochlear Implants International, 11(1):4-41.
7. **Litschel R , Majoor J, and Tasman A (2015):** Effect of Protruding Ears on Visual Fixation Time and Perception of Personality. JAMA Facial Plastic Surgery, 17(3):183.
8. **Byun S, Hong P and Bezuhly M (2016):** Public Perception of the Burden of Microtia. Journal of Craniofacial Surgery, 27(7):1665-1669.
9. **Carey JC, Park AH, Muntz HR (2006**): External Ear. In: Stevenson RE, editor. Human malformations and related anomalies. Oxford; New York: Oxford University Press,Pp329–338.
10. **Alasti F, Sadeghi A, Sanati M, Farhadi M, Stollar E, Somers T and Van Camp G. (2008):** A Mutation in HOXA2 Is Responsible for Autosomal-Recessive Microtia in an Iranian Family. The American Journal of Human Genetics, 82(4):982-991
11. **Suutarla S, Rautio J, Ritvanen A, Ala-Mello S, Jero J and Klockars T (2007):** Microtia in Finland: Comparison of characteristics in different populations. International Journal of Pediatric Otorhinolaryngology, 71(8):1211-1217.
12. **Canfield M, Langlois P, Nguyen L and Scheuerle A (2009):** Epidemiologic features and clinical subgroups of anotia/microtia in Texas. Birth Defects Research Part A: Clinical and Molecular Teratology, 85(11):905-913.
13. **González-Andrade F, López-Pulles R, Espín VH, Paz-y-Miño C (2010):** High altitude and microtia in Ecuadorian patients. J Neonatal Perinatal Med., 3:109:116
14. **Luquetti D , Heike C , Hing A , Cunningham M. and Cox T (2011):**Microtia: Epidemiology and genetics. American Journal of Medical Genetics Part A, 158A(1):124-139.
15. **Johns A, Lucash R, Im D. and Lewin S (2015):** Pre and post-operative psychological functioning in younger and older children with microtia. Journal of Plastic, Reconstructive & Aesthetic Surgery, 68(4):492-497.
16. **Tanzer RC (1977):** Reconstructive Plastic Surgery. 2nd edition. Philadelphia, Pa, USA: WB Saunders.

17. **Nagata S (1993):** A New Method of Total Reconstruction of the Auricle for Microtia. Plastic and Reconstructive Surgery, 92(2): 187-201.
18. **Brent B (1999):** Technical Advances in Ear Reconstruction with Autogenous Rib Cartilage Grafts: Personal Experience with 1200 Cases. Plastic & Reconstructive Surgery, 104(2):319-334.
19. **Reinisch J, and Lewin S (2009):**Ear Reconstruction Using a Porous Polyethylene Framework and Temporoparietal Fascia Flap. Facial Plastic Surgery, 25(03):181-189
20. **Kelley P, Hollier L, Stal S (2003**): Otoplasty: evaluation, technique, and review. J. Craniofac. Surg., 14 : 643e653
21. **Forrester MB, Merz RD (2004):** Impact of excluding cases with known chromosomal abnormalities on the prevalence of structural birth defects Hawaii, 1986–1999. Am J Med Genet., 128:383–388.
22. **Shaw GM, Carmichael SL, Kaidarova Z, Harris JA (2004):** Epidemiologic characteristics of anotia and microtia in California, 1989–1997. Birth Defects Res., 70:472–475.
23. **Forrester M, and Merz R (2005):** Descriptive epidemiology of anotia and microtia, Hawaii, 1986-2002. Congenital Anomalies, 45(4):119-124.
24. **Zhu J, Wang J, Liang J, Zhou G (2000):** An epidemiological investigation of anotia and microtia in china during 1988–1992. Zhonghua er Bi Yan Hou Ki Za Zhi., 35:62–65
25. **Castilla EE, Lopez-Camelo JS, Campana H (1999):** Altitude as a risk factor for congenital anomalies. Am J Med Genet., 86:9–14.
26. **Mallo M (2003):** Formation of the outer and middle ear, molecular mechanisms. Development of Auditory and Vestibular Systems 3: Molecular Development of the Inner Ear., 57:85–113.
27. **Harris J, Kallen B, Robert E (1996):** The epidemiology of anotia and microtia. J Med Genet., 33:809–13.
28. **Marx H (1926):** Die Missbildungen des ohres. In: Denker, AKO., editor. Handbuch der Spez Path Anatomie Histologie ,Berlin.Springer;Germany.
29. **Hunter A, Frias JL, Gillessen-Kaesbach G, Hughes H, Jones KL, Wilson L (2009):** Elements of morphology:standard terminology for the ear. Am J Med Genet A, a; 149A (1):40–60.
30. **Weerda H (1988):** Classification of congenital deformities of the auricle. Facial Plastic Surgery, 5(5):385–388.
31. **Tanzer RC(1978):** Microtia. Clin Plast Surg. , 5(3):317–36
32. **Nagata S (2000):** Microtia (auricular reconstruction). In: Achauer B,Erikkson E, eds. Plastic Surgery: Indications, Operations, Outcomes, 2:1023–1055
33. **Stoll C, Alembik Y, Dott B, Roth MP(2016):** Associated Anomalies in Cases with Anotia and Microtia. European Journal of Medical Genetics ,59(12):607-614
34. **Okajima H, Takeichi Y, Umeda K, Baba S (1996):** Clinical analysis of 592 patients with microtia. Acta Otolaryngol Suppl,52:18–24.
35. **Anderka MT, Lin AE, Abuelo DN, Mitchell AA, Rasmussen SA (2009):** Reviewing the evidence for mycophenolate mofetil as a new teratogen: case report and review of the literature. Am J Med Genet A,149A (6):1241–8.
36. **Klieger-Grossmann C, Chitayat D, Lavign S, Kao K, Garcia-Bournissen F, Quinn D, Luo V, Sermer M, Riordan S, Laskin C, Matok I, Gorodischer R, Chambers C, Levi A, Koren G (2010):** Prenatal exposure to mycophenolate mofetil: an updated estimate. J Obstet Gynaecol Can.,32(8): 794–7.
37. **Kaye CI, Rollnick BR, Hauck WW, Martin AO, Richtsmeier JT, Nagatoshi K (1989)**: Microtia and associated anomalies: statistical analysis. Am J Med Genet., 34(4):574–8.
38. **Mastroiacovo P, Corchia C, Botto LD, Lanni R, Zampino G, Fusco D (1995):** Epidemiology and genetics of microtia-anotia: a registry based study on over one million births. J Med Genet., 32(6):453–7.
39. **Heike CL, Luquetti DV, Hing AV (2009 Mar 19 [Updated 2014 Oct 9]):** Craniofacial Microsomia Overview. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle**;** 1993-2017**.Available from:** https://www.ncbi.nlm.nih.gov/books/NBK5199/
40. **Quatela V, Thompson S and Goldman N (2006).** Microtia Reconstruction. Facial Plastic Surgery Clinics of North America, 14(2):117-127.
41. **Bly R , Bhrany A , Murakami C and Sie K (2016).** Microtia Reconstruction. Facial Plastic Surgery Clinics of North America, 24(4):577-591.
42. **Romo T , Presti P and Yalamanchili H (2006):** Medpor Alternative for Microtia Repair. Facial Plastic Surgery Clinics of North America, 14(2):129-136.
43. **Cabin J., Bassiri-Tehrani, M. Sclafani, A. and Romo, T. (2014):** Microtia Reconstruction. Facial Plastic Surgery Clinics of North America, 22(4):623-638.
44. **Ebrahimi A, Kazemi, A , Rasouli H R, Kazemi M , & Kalantar Motamedi M H (2015):** Reconstructive Surgery of Auricular Defects: An Overview. *Trauma Monthly*, *20*(4): e28202.
45. **Romo T, and Reitzen S (2008):** Aesthetic Microtia Reconstruction with Medpor. Facial Plastic Surgery, 24(1) :120-128