# *USHER SYNDROME A REPORT STUDY OF A JORDANIAN FAMILY*

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## *Abstract*

Usher syndrome includes Retinitis Pigmentation (Pigmentosa) accompanied by hearing loss. The hearing loss is congenital , stable, and usually quite severe, although severity can vary in different individuals.

Usher syndrome is a recessively inherited condition. One of the greatest difficulties experienced by sufferers is the increased isolation as the restrictions on both spoken and visual communication increase .

Our study includes a family of six individuals, three of them were found affected with Usher. Two of them were found homozygous type II with moderate hearing loss, the third was found homozygous type I with profound hearing loss. The three affected children were audiologically rehabilitated with suitable hearing aids, accompanied with regular visual examination .

The study recommends the application of global hearing screening program for school children which will help in early identification of hearing disability, and its early management.

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# "متلازمة آشر": دراسة حالة لأسرة أردنية


## ملخص

"متلازمة آشر" هو مرض وراثي متنحى وأعراضه العمى والصمم، وهو ثلاثة أنواع، وقد هدفت الدراسة إلى الكشف المبكر عن الحالات المصابة بضعف السمع والتي تتسبب في الإعاقة الدراسية للأطفال، ومن ضمن أهم مسببات الإعاقة السمعية هي الامراض الوراثية ومن أشهر هذه الامراض الوراثية هي متلازمة آشر. وقد تم في هذه الدراسة فحص أسرة مكونة من ستة أفراد سمعياً في عيادات جامعة عمان الأهلية، وأجريت لهم فحوصات شاملة للبصر في أحد المستشفيات الخاصة المتخصصة في العيون بعمان وتم اخذ عينات للدم من جميع أفراد الأسرة وأرسلت بمرافقة الباحث إلى معمل الهندسة الوراثية التابع لكلية الطب بجامعة القاهرة للدراسة والبحث.

وقد أظهرت النتائج إصابة طفلين من الاسرة بالنوع الثاني للمتلازمة مع صمم متوسط الدرجة، وإصابة طفل بالنوع الأول مع صمم عميق الدرجة.

وبناء على هذه النتائج تم تأهيل الأطفال سمعياً بالمعينات السمعية المناسبة، مع المتابعة المستمرة للفحص والتأهيل البَصَري.

وتوصي الدراسة بضرورة تطبيق في رامج الكشف المبكر (للسمع والبصر) بالعمر المبكر للمحافظة على أطفالنا صحياً وتعليمياً.

# *Introduction*

Usher syndrome is the most common condition that involves both hearing and vision problems. Usher syndrome has other names used in practice ;

Dystrophia retinae pigmentosa-dystosis syndrome , Graefe - Usher syndrome,Hallgren syndrome, Retinitis pigmentosa - deafness syndrome.

The major symptoms of Usher syndrome are hearing impairment and retinitis pigmentosa, an eye disorder that causes a person's vision to worsen over time [5]. Some people with Usher syndrome also have balance problems [10]. There are three general types of Usher syndrome [14]; Usher syndrome type 1 (USH1), Usher syndrome type 2 (USH2) and Usher syndrome type 3 (USH3). USH1 and USH2 are the most common types. Together, they account for approximately 90-95 % of all cases of children who have Usher syndrome[5] .

Although the syndrome was first described by Albercht Von Graefe in 1858, it was named after Charles Usher, a British eye doctor, who believed that the condition was inherited or passed over from parents to their children. Sometimes genes are altered or mutated. Mutated genes may cause cells to act differently than expected.

Approximately 3-6% of all deaf children and perhaps another 3-6% percent of hard-of-hearing children have Usher syndrome[20]. In developed countries such as the United States, about 4 babies in every 100.00 births have Usher syndrome[15].

People with USH1 [6] are profoundly deaf from birth and have severe balance problems. Many of these individuals obtain little or no benefit from hearing aids. Most use sign language as their primary means of communication. Because of the balance problems, children

with USH1 are slow to sit without support and rarely learn to walk before they are 18 months old. These children usually begin to develop vision problems by the time they are ten. Visual problems most often begin with difficulty seeing at night, but tend to progress rapidly until the individual is completely blind.

Individuals with USH2 [6] are born with moderate to severe hearing impairment and normal balance. Although the severity of hearing impairment varies, most of these children perform well in regular classrooms and can benefit from hearing aids. These children most commonly use speech to communicate. The visual problems in USH2 tend to progress more slowly than the visual problems in USH1. USH2 is characterized by blind spots that begin to appear shortly after the teenage years. When an individual's vision deteriorates to blindness, his or her ability to speech and read is lost.

Children born with USH3 [6] have normal hearing and normal to near-normal balance. However hearing worsens over time, the rate which hearing and sight are lost can vary between affected individuals, even within the same family. Children develop noticeable hearing problems by their teenage years and usually become deaf by mid to late adulthood. Night blindness usually begins sometime during puberty. Blind spots appear by the late teenage years to early adulthood. By mid-adulthood, the individual is usually blind.

Special tests such as electronystagmography (ENG) detect balance problems and electroretinography (ERG) detect retinitis pigmentosa help specialists to detect Usher syndrome earier. Early diagnosis is important in order to begin special educational training programs to help the individual manage the combined hearing and vision difficulties.

## *Results:*

Three siblings were found to have hearing loss ,the eldest daughter ,the youngest daughter ,and the son as shown in table 1. These siblings were sent for ophthalmic examination

**Table (1) Audiologic findings**

| No. | Subject | Middle Ear Analysis | Diagnostic Audiometry | ERA ** |
|---|---|---|---|---|
| 1. | Father (F) | Bil. Type A * Preserved reflexes | Within normal hearing threshold | Not performed |
| 2. | Mother (M) | Bil. Type A Preserved reflexes | Within normal hearing threshold | Not performed |
| 3. | Daughter (D1) | Bil. Type A Absent reflexes | Bil. Moderate S.N.H.L. | Moderate Hearing loss |
| 4. | Daughter (D2) | Bil. Type A Preserved reflexes | Within normal hearing threshold | Not performed |
| 5. | Daughter (D3) | Bil. Type A Absent reflexes | Bil. Moderate S.N.H.L. | Moderate Hearing loss |
| 6. | Son (B1) | Bil. Type A Absent reflexes | Bil. Profound S.N.H.L. | No response at Max. threshold |

## *Aim of the study:*

The study aims to focus on one of the most serious ,congenital diseases that affects two main senses of human being , which are hearing and vision.

It shows a well organized plan for diagnosis of such cases including visual, audiological, and blood analysis.

## *Material and Methods:*

A family of 6 members were examined in the Audiology clinics of the Hearing department -Al-Ahliyya Amman University , for the first time on November 2005 . The family Tafilah is formed of a father ,a mother , and three daughters and one boy ( all from Tofilah district).

**The investigations used in study are Audiologic**: To detect the presence of sensory-neural hearing loss, and assessing its degree whither mild, moderate or severe.

The equipments used for hearing assessment are:

1. Middle Ear Analyzer (GSI Tymp Star Version 2)
2. Diagnostic Audiometer (Amplivox 270)
3. Auditory Evoked Potential (AEP) System, Biologic Systems Corp.

**Ophthalmic** :To assess field of vision, presence of nyctalopia (Night Blindness) & retinal degeneration (Retinitis Pigmentosa) using ophthalmoscope. Also the presence or absence of Electro-Retino-Gram (ERG) .

**Blood sampling**: For Gene Localization of Usher syndrome, the samples taken from all family members (affected & non affected). Part of the blood sample is used to establish permanent lymphostoid cell lines.

* Bil .Type A= bilateral normal middle ear pressure

**ERA =evoked response audiometry

**Table (2) Ophthalmic findings**

| No. | Subject | ERG | R. P. | Field of Vision |
|---|---|---|---|---|
| 1. | D1 | Present | Starting Pigmentation & Tortuous Retinal vessels | Narrow vision |
| 2. | D3 | Present | Abnormal Retinal vessels | Slightly affected vision |
| 3. | B1 | Absent | Present & excessive | Bil. 20/160 Poor vision |

**Table (3) Blood sample findings (two Lod scores for Usher syndrome)**

| No. | Subject | Type I Marker | Type II Marker | Type III Marker |
|---|---|---|---|---|
| 1. | F. | Weak + ve | - ve | - ve |
| 2. | M. | - ve | Weak + ve | - ve |
| 3. | D1 | - ve | + ve | - ve |
| 4. | D2 | - ve | - ve | - ve |
| 5. | D3 | - ve | + ve | - ve |
| 6. | B1 | Strong + ve | - ve | - ve |

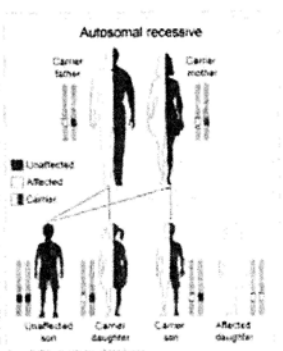
The Lod scores from the two point analysis of each marker locus with Usher syndrome types are shown in table (3)

**Table (4) overall cumulative findings**

| No. | Subject | Age | Complaint | Audiologic | Ophthalmic | Genetic |
|---|---|---|---|---|---|---|
| 1. | F | 48y 3 m | None | Normal | Not done | Heterozygous type I |
| 2. | M | 37y 4 m | None | Normal | Not done | Heterozygous type II |
| 3. | D1 | 16y 1 m | Hearing & visual loss | Moderate hearing loss | Retina & vision affected | Homozygous type II |
| 4. | D2 | 14y 6 m | None | Normal | Not done | Homozygous free (unaffected) |
| 5. | D3 | 8y 3 m | Hearing & visual loss | Moderate hearing loss | Retina & vision affected | Homozygous type II |
| 6. | B1 | 1y 10 m | Hearing & visual loss | Profound hearing loss | Retina & vision affected | Homozygous type I |

## *Discussion:*

Usher is transmitted genetically by autosomal recessive gene Fig. (1). There are three genetic types of Usher (4,5,6,7,8)




Usher syndrome is inherited in an autosomal recessive pattern.

Figure (1)

As shown in figure 2, (autosomal recessive pedigree ) ,the parents are first cousins . The father (F) is heterozygous type I, not showing the condition. The mother (M) is heterozygous type II, not showing the condition. The eldest daughter (D1) is homozygous type II, showing the condition .The 2nd daughter (D2) is homozygous free not showing the condition. The 3rd daughter (D3) is homozygous type II, showing the condition. The son (B1) is homozygous type I, showing the condition.

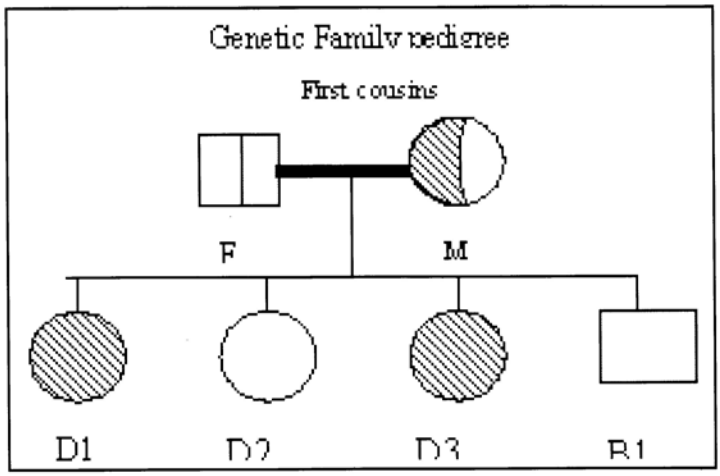



Figure (2)

Comparing our results with reviewed articles(1,2,3,)and published similar cases (5,7,8,) similarity is found as an autosomal recessive pattern but the study shows a unique combination of both types (I & II) in the same family inheritance pedigree not found in other researches 1,2,3,4,5,6,7,8.

## *Conclusion and Recommendations*

Three siblings were found to have Usher syndrome .

The study encourages the Genetic Counseling especially in cases of relative marriages for early prevention of this mode of inheritance.

Sub typing of Usher syndrome cases would help to mark each type in the appropriate education and training level , that makes the individual as positive participant in community and minimizing the consequences of the syndrome. After diagnosis specific rehabilitation programs were tailored for each case.

The study also encourages early Cochlear Implantation such cases for better prognosis (type I), saving at least one of the two affected senses.

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