Meckel Syndrome, Type 1

**Alternative Names**
- MKS1
- Meckel Syndrome
- MKS
- MES
- Dysencephalia Splanchnocystica
- Gruber Syndrome
- Meckel-Gruber Syndrome

**WHO International Classification of Diseases**
- Congenital malformations, deformations and chromosomal abnormalities

**OMIM Number**
- 249000

**Mode of Inheritance**
- Autosomal recessive

**Gene Map Locus**
- 17q23

**Description**
Meckel syndrome is a major autosomal recessive monogenic malformation syndrome with a neural tube defect leading to death of the fetus in utero or shortly after birth. It comprises of a classical triad of occipital meningo-encephalocele, infantile polycystic kidneys, with multicystic dysplasia and fibrotic changes in the portal area of the liver and with ductal proliferation, and postaxial polydactyly. Other features include facial clefts, microcephaly, cerebellar and cerebral hypoplasia, hydrocephalous, sloping forehead, congenital heart disease and pulmonary hypoplasia. Genital anomalies are hypoplastic penis, cryptorchidism, Mullerian-duct remnants and epididymal cysts in males. Septate vagina and hypoplastic or bicornuate uterus may, be associated in females. Pulmonary hypoplasia is the leading cause of death. The incidence of this syndrome worldwide varies from 1 in 13,250 to 1 in 140,000 live births.

**Molecular Genetics**
Type 1 Meckel syndrome loci have been mapped to chromosome 17q22-q23. The HOXB gene cluster is located nearby at 17q21-q22 and abnormalities of some of the HOXB genes in mice lead to multiple malformations bearing some parallels to the Meckel syndrome phenotype.

**Epidemiology in the Arab World**

**Egypt**
Teebi and Teebi (2005) indicated that Meckel syndrome is frequently diagnosed in Egypt.

**Kuwait**
Farag et al. (1990) described five Bedouin sibs with Meckel-Gruber syndrome. Each affected sib manifested only two of the three cardinal signs of the disease: occipital encephalocele and polycystic kidneys, lacking polydactyly. Teebi et al. (1992) and Teebi (1994) further emphasized the observation that Meckel syndrome is commonly encountered in Kuwait; especially the Bedouin population.

In a review of genetic diversity among Arabs, Teebi and Teebi (2005) indicated that Meckel syndrome has a prevalence of 1:3500 live births in Kuwait.

**Palestine**
Al-Gazali et al. (1996) reported a child, born to unrelated parents of Palestinian-Jordanian origin, with typical features of Meckel syndrome in whom both encephalocele and Dandy Walker malformation (DWM) existed. This female child, as well as two previous females born to the family, were born with posterior encephalocele, polycystic kidneys and no polydactyly. Both died a few hours after birth. At birth, the propositus was noted to also have wide sutures with an occipital encephalocele. CT scan of the brain showed
hypoplastic cerebellar hemispheres, an absent vermis and a very large posterior fossa cyst communicating with the fourth ventricle, and high attachment of the tentorium. Renal ultrasound showed hugely enlarged hyperchogenic kidneys on both sides with loss of corticomedullary differentiation. The baby died on the second day of life.

In 1997, Zlotogora (1997a) analyzed 2000 Palestinian Arabic families and found that in 98 families at least one individual had congenital hydrocephalus and/or open neural tube defect. In 22 families the brain malformation was part of a syndrome: Meckel syndrome in 10, Warburg syndrome in another 5, Carpenter in one, and undiagnosed in 6 families. In the case of patients with Meckel syndrome, the parents were consanguineous and in six as first cousins. In these families, 17 individuals were affected: Five with hydrocephalus alone, six with occipital cephalocele, and six who died at home without exact description of the cranial defect.

Zlotogora (1997b) conducted a survey of 2000 different Palestinian Arab families. In 601 cases, an autosomal recessive disease was diagnosed or strongly suspected. The distribution of these disorders was not uniform and some disorders, such as Krabbe disease, were found at high frequency in only a small part of the population. For some other disorders, a high prevalence was also reported among Palestinian Arabs living in other regions, for example, beta thalassemia, Bardet-Biedl syndrome, Meckel syndrome, autosomal recessive congenital hydrocephalus, and recessive osteopetrosis.

In a review of genetic diversity among Arabs, Teebi and Teebi (2005) indicated that Meckel syndrome has a prevalence of 1:2000 live births in Jerusalem.

**Saudi Arabia**
Ramadani and Nasrat (1992) reported a rare case of Meckel-Gruber syndrome in a woman who had three affected offspring in the past with similar condition.

Patel (1992) evaluated 17 patients, age 1 day to 6 years with infantile polycystic kidney disease with ultrasound and other imaging techniques. Most patients showed bilaterally enlarged kidneys with hyperechoic renal parenchyma, which had poor differentiation in outlines as well as between renal sinus, cortex and medulla. Few rare findings such as liver cysts, associated Meckel syndrome, renal stone, bilateral vesicoureteric reflux and renal calcification were also noted.

Teebi and Teebi (2005) indicated that Meckel syndrome is frequently diagnosed in the Arabian Peninsula.

**Tunisia**
Boutheina et al. (2000) carried out 43 prenatal diagnoses of lethal urinary tract abnormalities during a five-year-period. The abnormalities encountered included bilateral renal agenesis (56%), autosomal recessive polycystic kidney disease (16%), autosomal dominant polycystic kidney disease (14%), Meckel-Gruber syndrome and Prune-Belly syndrome (4%). The pregnancy was interrupted in 35 cases (81.4%).

**United Arab Emirates**
Al Talabani et al. (1998) studied the pattern of major congenital malformations in 24,233 consecutive live and stillbirth at Corniche hospital, which is the only maternity hospital in Abu Dhabi, between January 1992 and January 1995. In this period, a total of 401 babies, including 289 Arabs, were seen with major malformation. Chromosomal anomalies accounted for 19% of the cases, single gene disorders for 24%, of which 19% were due to autosomal recessive disorders. The multifactorial conditions were 26% of the cases, and the sporadic conditions were 26% as well. In their study, Al Talabani et al. (1998) observed 4 cases of Meckel syndrome born to consanguineous parents. Recurrence of the disease was also reported. Al Talabani et al. (1998) concluded that their study was very close to representing the true incidence of congenital abnormalities in the whole United Arab Emirates, as they investigated over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

**References**


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