Prevalence of Corneal Dystrophies in the United States: Estimates from Claims Data

This one-year-old paper by Musch et al.\(^1\) raises a very intriguing question, which, however, is hardly answered beyond any doubt.

A shortcoming of this paper is the lack of discussion of the diagnostic specificity. Who diagnosed these patients? Was it a cornea specialist, a general ophthalmologist, or an optometrist? Are the diagnoses clinical? Have they been verified by family investigations, and in how many generations? Have they been verified by electron microscopy or histology? Have they been tested in a genetic lab?

From personal experience\(^2\) and from discussions in the International Committee of Classification of Corneal Dystrophies (IC3D),\(^3\) it is obvious that even among highly devoted cornea specialists with an interest in corneal dystrophies, their clinical impression of some dystrophies does not always correlate with a correct diagnosis.

Musch et al.\(^1\) found that the most frequent entity was endothelial corneal dystrophy. As mentioned briefly in their paper, and as stressed in the IC3D paper,\(^2\) most cases named endothelial corneal dystrophy are not genetic, but probably comprise an etiologically heterogeneous group of diseases of a degenerative nature. These diseases are therefore not true dystrophies. They should not be included in a paper that attempts to describe the prevalence of corneal dystrophies. One of the main purposes of the new IC3D classification was to define which entities are true, genetic, dystrophies. The authors, subsequently, describe groups that are “unspecified” and “anterior,” both of which comprise unknown entities. These groups are too vaguely defined to have scientific impact. This leaves around 900 dystrophy patients (from among 27,000 enrollees) distributed over only 4 diagnoses of the 25 IC3D classified corneal dystrophies. There is no attempt to discuss why the remaining dystrophies are not recognized in the material of 8 million patients. Musch et al.\(^1\) also discuss prevalence among different ethnic groups. The importance of this is doubtful, as one does not know how many new mutations have occurred, and in a genetic melting pot like the United States, which ethnic group originally harbored the mutation. A specific mutation may prevail in one ethnic group in the family tree, only to be interpreted to belong to another ethnic group few generations later.

The authors state that women predominate among all patients with corneal dystrophies. Is this relevant when most dystrophies are inherited as autosomal traits? Is this really sex-dependent penetrance? Or does this fact show that there is bias?

The authors have estimated the mean age for macular corneal dystrophy at 47.3 years, and that many patients have had their keratoplasty after the age of 45. This calls for some discussion, as most sources describe that visual acuity in macular corneal dystrophy has already been dramatically affected in the 20s.

Finally, prevalence (or incidence) is not an ideal way to describe frequency among these kinds of inherited diseases. The paper correctly describes that some entities are more frequent in some areas, one example from the United States is Schnyder corneal dystrophy.\(^4\) This is due to the founder effect, that is an increase in the number of cases due to a new mutation in a (isolated) population.

Ideally, the best way of describing these inherited diseases is to calculate the mutation rate for each dystrophy. This is the only way to compare the frequency of different dystrophies among (different) populations independent of family structure, survival rate, and socioeconomic environment. It is also independent of the number of generations a specific mutation has been around in the area(s) under consideration. However, this has almost never been done, and the only one suggestion of a mutation rate\(^2\) is definitely not the whole truth. Whether it is actually possible to work out the mutation rate is doubtful.

Prevalence and incidence are probably also too difficult to work out as most of these conditions are so rare, and the founder effect gives a bias. In Denmark, with a population of 5 million people, several of the 25 classified corneal dystrophies have never been seen by the corneal dystrophy specialists, and probably nobody is able to survey all of the 511 million people in the U.S.

Finally, we do appreciate that Musch et al.\(^1\) were aware of the difficulty of the subject and that the authors actually commented that the study design did limit conclusions that could be drawn, however we do not agree with the interpretation of the observations as presented.

Hans Ulrik Møller\(^1\)
Lone Sunde\(^2\)

\(^1\)Department of Pediatric Ophthalmology, Viborg and Aarhus Hospitals, Viborg and Aarhus, Denmark. \(^2\)Department of Clinical Genetics, Aarhus University Hospital, Aarhus Denmark. E-mail: hans.ulrik.moeller@viborg.rm.dk.

References


Citation: Invest Ophthalmol Vis Sci. 2013;54:387. doi:10.1167/iovs.12-11211