How cousin marriages can wreak genetic havoc on children

If you ever want to see some fascinating genetic disorders, you should all travel to Pakistan.



his is how my genetics professor started off her workshop class with us, during one of the courses in my postgraduate degree in the UK. The workshop dealt with the challenge of examining a particular genetic disorder – and searching for its probable roots. During the course of the workshop, she offered a range of cases, including a family with six children, four of whom

suffered from depression, schizophrenia or hearing problems. Of the 10 cases she shared with us, five of them were Pakistani patients and all of them came from cousin marriages.

In more technical language, these are called consanguineous marriages – unions between individuals that are related to each other as either second cousins or closer. There are different degrees of consanguinity, where the first-degree is your parent or your child, a second-degree relationship includes siblings, grandparents and grandchildren, third-degree has aunts/uncles, nieces/nephews, great-grandparents while the fourth-degree also includes first cousins.

These unions hold the potential to create significant genetic issues in nations such as Pakistan, where a <u>recent study</u> estimated that more than 60 percent of the population carries out such marriages. The situation has prompted lawmakers there to pass new <u>legislation</u> aimed at forcing related couples to seek genetic screenings to fight the rising incidence of a hereditary blood disorder and to raise awareness about the dangers of cousin marriages.

Under the <u>Roman civil law</u>, individuals were forbidden to marry anyone within the four degrees. Because of that, cousin marriages started interchangeably being used with inbreeding or incest and therefore became less common in the west. The same beliefs were not pushed in parts of South Asia and the Middle East, where Islam was the predominant religion and only restricted marriages to the third degree. Thereby cousin marriages not only became a common practice but in time also became a cultural norm that is now actively promoted and preferred in most of those regions.

From a genetics standpoint, the <u>link</u> between these cousin marriages and increased risk of genetic disorders in the offspring of such marriages has become strong. The reason for that is in the laws of probabilities. The causes behind the differences between individuals, is mostly due to recombination of genes during the process of meiosis in cells. Other than that, mutational events and independent assortments also cause genetic variations, that differs one individual from the other. However, these variations are of a very small percentage as all humans share roughly 99 percent of their genomes with others. It's the approximate one percent that brings about the differences between us.

Looking at the average DNA that is shared among relatives, a person shares 50 percent of their DNA with their parents and 50 percent with their siblings. As the degrees shift from 1st to 4th, the percentage of shared DNA drops whereby you end up sharing 12.5 percent of your DNA with your first-cousins.

That shared DNA is significant when those cousins inter-marry. The problem is that the common gene pool from which genetic variation arises becomes smaller and smaller the more one marries within a family. And through such restricted genetic pools, the recessive genes that cause autosomal recessive disorders become dominant and get expressed in the offspring.

The chance of carrying a dangerous allele is slim. However, in these marriages, both cousins share the same set of grandparents. If one grandparent carries a dangerous allele, then there is a 50 percent chance the child of the grandparent (cousin's parent) becomes a carrier. This increases the chance that the offspring of the cousin will get two copies of the dangerous allele.

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According to various published <u>studies</u>, a variety of disorders have been linked to this breeding practice, including <u>congenital heart disease</u>, blood diseases such as hemophilia and thalassemia, deafness, cystic fibrosis, breast cancer and depression.

Looking at hemophilia in a closer light, the link between this blood disorder and the royal British family has been widely discussed. <u>Royal families</u> were notorious for their cousin marriages (or interbreeding) in order to preserve their lineage and to keep the royal blood 'pure'. However, the consequences of such interbreeding were devastating, as seen elsewhere in Europe.

Consider the <u>Habsburg</u> family of Spain. The family possessed the gene for mandibular prognathism, a genetic disorder that causes the lower jaw to outgrow the upper jaw leading to a pronounced chin. In the Habsburg family, this condition persisted and kept getting more pronounced through generations of interbreeding. The condition became so pronounced in <u>Charles II of Spain</u> that he was not able to chew his own food. Along with this deformity, there were a number of other genetic, physical and intellectual problems that he faced. What this tells us is that the condition existed within the genetic makeup of the Habsburg family and became continually worse through interbreeding.



Charles II of Spain. Image: Wikipedia.

That is the case with how rare recessive disorders show up in the offspring of interbreeding families, primarily because of the restrictions it places on the available gene pool. And yet, the genetic downside of these unions doesn't weigh against the cultural and societal positives that such cousin marriages seemingly bring for families, particularly in the Middle Eastern and South Asian region.

The main reason behind the popularity of cousin marriage is two-fold. First, it provides financial security by assuring that property or monetary assets stay within a family. Second, it offers personal security for parents who want to see their sons or daughters married to trusted spouses, rather than strangers. This especially holds true in the rural areas of Pakistan where there is limited education and awareness regarding the harms of cousin marriages. Before people can understand that marrying one's cousin can be harmful to their offspring, they need to first understand what genetics is, how diseases can get passed within the family and how this knowledge can empower their choices and decisions.

One step towards this awareness was taken by <u>news</u> of a legislative bill being passed by the Pakistani government, regarding the blood disorder Thalassemia. The bill now makes it mandatory for a Thalassemia screening test to be taken by couples before they can get married. The hereditary disorder causes an excessive destruction of red blood cells leading to anemia. In Pakistan alone the rate of being a carrier for this disorder is 3 to 5 percent. It is estimated that approximately 10 million people in Pakistan suffer from this disorder. The hope is that through the mandatory screening, a solid prevention method will not only halt this disorder from being continuously passed on but will also raise awareness regarding hereditary disorders themselves.

This is a crucial step taken by the country, a step needed towards a goal that ultimately gets the message

across regarding the importance of preventing the spread of genetic disorders. These marriages aren't the root cause of these various genetic disorders. But they are responsible for the increased risk of developing these disorders. And if those risks can be lowered, numerous cases of offspring's born with deformities or cases of fetal mortality can also finally be managed.

Mariam Sajid has a masters degree in molecular genetics and is passionate about improving medical communications that aims to effectively translates scientific advancements to the public. Follow her on her blog.

This article was originally published at the GLP on April 10, 2019.