DOWN SYNDROME IN THE ARAB WORLD

Down syndrome is one of the most common chromosomal anomalies affecting approximately 1 in every 800 births, although higher incidence rates occur with increasing maternal age. The underlying genetic cause of this disorder is having an abnormal number of chromosomes in the cell. Chromosomes carry the cell's genetic information and they are normally grouped in 23 pairs making up a total of 46 chromosomes, half of which comes from the mother and half from the father. Importantly, the number of chromosomes in the case of Down syndrome is 47 instead of 46; this is due to having one extra chromosome (number 21) in addition to the normally existing pair (one from each parent). This is why Down syndrome is also referred to as "trisomy 21"; i.e. having three chromosomes 21. However, the disorder can also be caused by partial trisomy, which results from harboring one extra copy of ***part*** of chromosome 21 attached to another chromosome. Deviations from the correct number of chromosomes, as in the case of Down syndrome, originate mostly from errors in distributing chromosomes between dividing cells during the formation of the egg or the sperm. Such errors can also take place after fertilization; so that some cells will have the correct chromosomal number while others don't, which makes the resulting embryo a "mosaic". Individuals with a mosaic cell pattern may have a less pronounced version of Down syndrome.

Down syndrome is readily recognizable because of the characteristic physical features that accompany the disorder. Perhaps the most noticeable of these features is the eyes; which are more than normally distant from one another and the inner corners of the eye displaying oblique eye fissures. This, as well as having a flat nasal bridge, led to associate this disorder with a certain race (East Asians), hence the name "Mongolism". Unfortunately this offensive and misleading term is still widely used in common parlance in various Arab countries. Moreover, few medical professionals use "Mongolian Idiocy" to refer to the most prominent symptom of this disorder; impaired cognitive development. In addition to distinctive facial features and cognitive impairment, Down syndrome is associated with delayed growth, joint laxity and certain consequences of incomplete organ formation. Therefore it is high time these important issues of Down syndrome were raised in the Arab world on the 8th anniversary of World Down Syndrome Day on 21 March 2013.

The Centre for Arab Genomic Studies, through its Catalogue for Transmission Genetics in Arabs (CTGA) Database, continues to assemble and analyze research findings pertaining to genetic disorders in Arabs. Among these is Down syndrome which has understandably attracted notable scientific attention in numerous Arab countries such as UAE, Egypt, Kuwait and Oman.

Research data from nine different Arab countries feature in the CTGA entry for Down syndrome (DS). Covering periods that stretch over late 20th century to early 21st. Studies strongly indicate that in six of these countries the incidence of DS is higher than international figures. For example, DS incidence rate among UAE-nationals in Dubai is 1:319, which is slightly higher but comparable to figures from neighboring countries such as Oman (1:500) and Qatar (1:546). Similarly, Saudi Arabia and Kuwait are also on the higher end of international incidence rates with 1:554 and 1:581 respectively. Arabs in Israel also display a higher incidence rate (1:547), although termination of pregnancy in 35.7% of the cases led to less actual live births with DS.

Higher incidence in DS in Arab countries has been attributed to a number of factors including the widely-spread practice of consanguineous marriages, increased maternal age and having a high number of children. Other factors involve partial or complete lack of prenatal detection which can aid parental decisions to terminate pregnancies with DS fetuses. That said; the latter practice is not without problems and controversies. Some of these factors are strongly linked to the current socioeconomic state in the Arab world while others are to do with religious beliefs and convictions.

Marriages among first cousins are quite common in Arab countries, especially in the above-mentioned ones. In fact, almost all studies reporting high incidence of DS in a particular country hint to possible links with high consanguinity indices in that country. The Centre for Arab Genomic Studies (CAGS) reviewed overall consanguinity in Arabs in the last decade; the values were 56.3% in Oman, 42.1-66.7% in Saudi Arabia and 22-54% in Qatar. Specialists believe that distributing the right number of chromosomes between dividing cells is controlled by certain genes, disruption of which can lead to errors such as these underlying DS. So the tendency to give birth to babies with chromosomal abnormalities may be looked at as many other heritable disorders, i.e. it manifests itself more with intermarriage and endogamy. In fact, a highly interesting study from

Kuwait showed the relative risk for closely related parents to have babies with DS was four-fold higher than that for unrelated parents.

The risk of having a baby with DS and other chromosomal abnormalities clearly increases with maternal age. For instance this risk is less than 1:1000 at the age of 30 while it becomes 1:400 at the age of 35. Increased maternal age in the Arab world is linked to a number of social and economic trends. More Arab women opt for a good level of professional development in their 20s to early 30s as opposed to abandoning education and work prospects to start a family. The reasons and results of this phenomenon are hard to dissect but they revolve around providing better economic conditions for the family. These trends were observed in the western world throughout the shift to industrialization, and many approaches were taken there in order to deal with the challenges that emerged because of these trends. These approaches include: antenatal screening using ultrasound, blood tests, amniocentesis and chorionic villus sampling as well as preserving the oocyte (in an egg bank) for later fertilization. Now that the Arab world is experiencing similar trends, a thorough consideration should be given to these practices/measures and select what is appropriate in order to apply in our countries on a wider scale.

A quick look at the research findings in CTGA reveals the long list of serious complications that are associated with this disorder and their prevalence rates in the Arab world. These findings corroborate with results from international studies, albeit a study in Oman showed higher frequencies of complications such as congenital heart disease were observed in populations with high consanguinity indices (such as Arab countries). In general DS complications were listed in studies from Egypt, Bahrain, Kuwait, Palestine, Qatar and Lebanon and these include acute leukemia and impairment of cellular immune responses (increased susceptibility to infections), congenital heart disease (heart septal defects) as well as other complications that are mentioned in detail in the CTGA entry for Down syndrome.

Undoubtedly the burden of Down syndrome is immense on both patients and the society as a whole. It is important to keep in mind that the mental impairment associated with DS as well as other symptoms vary considerably from case to case. The individuality of DS patients is of massive importance when considering provision of education, social and healthcare on a large scale. In many countries the universal answer was and still is collective institutionalization, which was detrimental to many patients who could have developed and integrated socially. This was not to happen in Arab countries because the family is at the centre of society. Patients with disabilities are usually taken care of within the family, which can have a positive impact on the patient. However, this can also lead to major problems due to lack of professional help and the paucity of resources. Fortunately the world has come a long way in terms of raised knowledge and awareness about DS in many countries around the world, but still there is plenty of room for improvement. For that more retrospective and prospective research needs to done regarding all the complicated aspects of DS. Such research can help devising the best of protocols and approaches to meet the challenges imposed by this troubling disorder. And needless to say that with all the aforementioned population characteristics, Arab countries are in dire need to address these issues sooner than later.

Centre for Arab Genomic Studies

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