

Recent advances in Down's syndrome

Abstract

The perception and management of Down's syndrome has evolved. The taboo about these babies, who are unfortunate, not because of any fault of theirs, is increasingly eroding. For many of those who survive life in-utero, who are a small fraction of those that are aborted spontaneously or induced, life expectancy appears to be increasing, and the global perception appear to be changing for good. Some have been known to live fairly qualitative life and are involved in in campaigns for the society to recognize that there is a place for them in the world. Here, the author reviews recent scientific evidence, management trends and societal debate.

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Anthony Emeka Madu

Obstetrics and Gynaecology, RCOG/FSRH/1 LM, UK

Correspondence: Anthony Emeka Madu, Specialist Registrar, Obstetrics and Gynaecology, RCOG/FSRH/1 LM, UK, Tel +44-793-162-6315, Email emimadu@yahoo.co.uk

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Introduction

The new prenatal test for Down's syndrome (trisomy 21) provides difficult choices for prospective parents. The screening test is offered routinely. However, some prospective mothers, who are in the minority, chose not to have the test. For those with positive screening test, the next step would be a confirmatory test if they wished to take that route. However, some parents chose not to, stating the outcome would not affect their love for their unborn babies. Some campaigners agree with this stance adopted by this group of parents and use alarming terms in their campaigns; like 'eugenic' or 'eradication', to describe the termination of pregnancy (TOP), following a positive confirmatory test.

Emotive language has been presented to a US Congressional hearing which laid bare ethical ramification of prenatal screening. A Down's syndrome sufferer and activist argued at the US Congressional hearing, that there appeared to be no place on earth for people with disability. In reality, it is not their fault that they are the way they are. In many western countries, women have the right to abort their pregnancies at certain gestational age limits even without the unborn baby having Down's syndrome. In other branches of Healthcare, more information to patients or clients is usually regarded as a good practise, as it leads to informed choices. In current obstetrical care, many argue such options are not robustly offered. Many activists raise strong objections at targeting and killing a group of people simply because of their disability. This once again raised the question of where the balance in this global discourse lies.

According to an article by Wilson C, 2018, 66% of pregnant women in the UK take up the Down's syndrome screening and 90% of women who get a positive screening test result opt for TOP.¹

Background information

This syndrome is caused by non-dysjunction at DNA duplication at chromosome 21. This compromises fetal development leading to characteristic facial anomalies or atypical facies; varying degrees of cognitive disability and higher risk of cardiac and other medical problems. As this extra chromosome is tested in pregnancy, it means that this syndrome is featured in debates around the world. This debate has in some parts of the world escalated to a new level, leading to protective legislations to protect these people.

In the US State of North Dakota, it is illegal for a doctor to terminate

pregnancy because of Down's syndrome. Legislatures in the states of Indiana, Louisiana and Ohio did same before the courts blocked the legislations. In Utah, the legislature is reported to be considering a bill in relation to the same matter.

Kurt Kondrich, a retired Police officer, and a father whose daughter suffers the disorder, told a UN panel that aborting babies with the disorder has become genocide. He argued that this was a prenatal death sentence meted out to completely innocent individuals.² Nuncio to the UN, Archbishop Bernardito Auzas, was reported as saying that people with the disorder are the happiest of people alive.²

In Ireland, a catholic country and one of the few countries in Europe where all forms of abortion was illegal, had its referendum on 25 May 2018. The "No" to abortion campaign had argued that legalizing abortion amounted to a stated sponsored eugenics programme for fetuses with Down's syndrome. The referendum was said to be a test of Ireland's catholic declining identity. Ireland was expected through the referendum decide whether to liberalize its strict abortion laws or not. The referendum was in relation to the repeal of 8th Amendment of the constitution passed in 1983 which established the right of the unborn child on a par with its mother.³ Ireland is known to have perhaps the most strict abortion laws in Europe, permitting abortion only when the life of the mother is at risk. At the final count, after all the results from the 40 constituencies had been analysed, the final result was as follows:

- YES 66.4% (drop the eight amendments)
- NO 33.6% (keep the eight amendments)
- Turn out 64.1%

This was a resounding 'Yes' vote this time, as two-thirds of voters backed the change, a position backed by the government during the campaign. Leo Varadkar, the Irish PM has promised new legislation by the end of the year. The legislations would permit abortion up to 12 weeks gestation; on demand and abortion after 12 weeks on medical grounds, the latter simulating that of UK provisions of conducting abortions on medical grounds. It would be interesting to know what the outcome of the referendum would be and its implications now and in the future.

In the UK, a new prenatal test to be introduced this year in England and Wales has brought this sensitive and emotive debate to the spotlight once again.

The current test has the following features:

- i. Requires screening blood test and ultrasound scan which only show increased chance of having the disorder.
- ii. Confirmation test is performed by chorionic villous sampling which has a 1% risk of miscarriage.
- iii. The latest test has the following features:
- iv. It analyses fetal DNA retrieved from maternal blood.
- v. There is no risk of miscarriage compared with the current prenatal confirmatory test.
- vi. It is much less invasive compared with the current prenatal confirmatory test.
- vii. It is 99% accurate.
- viii. It can be performed at 10 weeks gestation.

Impact of the new test

This is yet to evolve. More women are likely to take up the new screening test and have TOP. This, some argue could lead to less number of children with of Down's syndrome with consequences of less societal acceptance of those surviving with the disorder.

Campaigners warn of a trend towards an Iceland-like scenario where almost every pregnant woman with the diagnosis would have TOP. The high rate of TOP in Iceland had depended on the standard test and this new test is said not to be yet available in Iceland. Thus, in Iceland and in UK, there appear to be some uncertainty of the impact of this new test in relation to TOP and other related issues. In the UK, it is reported that 90% of pregnant women who gets a Down's syndrome diagnosis have a TOP.

An analysis suggest that the predicted higher take up rate of the new blood test would lead to 100 more diagnosis a year, and opponents of abortion say it would lead to 90 extra TOP. By implication, the number of babies born with Down's syndrome would drop from 710 to 610. Opponents of abortion argue that people with the disorder should be thought of as protected minority and that not enough is being done to protect these members of the society.

However, researchers found in 2015 that the 90 extra TOP stated earlier could well be an exaggeration: Though more women took the test, only 63% of those with positive test had TOP, suggesting that many of the extra women who opted to have the screening test were in fact not planning for TOP but only wanted to know what the situation was so as to make preparations.

According to researchers, the 90% TOP rate ignored the fact that only 66% of women took up the screening test in the first place. This clearly suggested that some of these women were put off by the 1% risk of miscarriage in relation to the process of confirmation of the disorder, while others would not mind having a child with the disorder. The number of people in the UK with Down's syndrome has doubled. It was 3:10000 in 1950, and 6:10000 in 2010. This suggests that fears about the decline of their population in the society, are unfounded. The rise in this number can be attributed to the following factors:

- A. People start families later in live these days.
- B. Improved medical care from advances in medical care.

Opponents of abortion also argue that all forms of medical screening are supposed to offer choices but in the case of Down's syndrome screening, parents say they are only encouraged to take up TOP.

One in 700 babies born in the U.S. or about 6,000 infants a year, according to Berman have this disorder.⁴ According to the US National Down Syndrome Society (NDSS) notes, "the effect is usually mild to moderate and is not indicative of the many strengths and talents that each individual possesses nonetheless." People with Down syndrome live full, rich lives, though statistically, they have a reduced life expectancy of about 60 years. However, things are getting better as in 1985; life expectancy was only 25 years, according to Berman.⁴

Current trends in care

Public Health England is said to be improving training for staff involved in the screening process to offer balanced counselling which emphasises positive and negative aspects of the disorder and use of proper respectful language.

Leaflet on Down's syndrome now state "chance" of having Down's syndrome and not "risk" of having Down's syndrome, the former being a more sensitive and respectful language.

In Ireland, Down's syndrome Ireland was reported to be against the use of affected babies in exploitative anti-abortion campaigns. Pro-abortion campaigners argue that the use of exploitative tactic was unfair to the women affected.

In the UK (Northern Ireland excluded), a woman can take up TOP before 24 weeks gestation if it would cause her distress. Such distress could, as some say, be anything including relationship break-up, financial distress or hardship, and so on. Some people therefore argue that having a baby with severe life-long disability must be a valid reason to take up TOP

In the UK, where the usual 24 week limit applies, Down's syndrome fetuses are treated differently as TOP can be performed till the end of pregnancy if the fetus was shown to have severe mental and physical disability. The upper chamber of the UK government was said to be considering a bill to remove the latter longer time limit of abortion. Though as some say it was unlikely to become law for reasons that are understandable, it will surely re-ignite the debate on Down's syndrome and abortion.

Iceland is said to be reviewing same longer time limit with a view to exemption. Currently there is growing rights for the disabled in the society and the two powerful opposing sides of the debate will surely collide again and again.

Then enter the green tea extracts

Children with Down's syndrome if given green tea from infancy are less likely to have the facial feature of the disorder according to a study.⁵ However, there has no safe dose has yet being determined.

A study according to the author suggests that excess of the enzyme, DYRK1A; appear to be responsible for some of the facial features of the disorder. Green tea contains epigallocatechin-3-gallate (EGCG) which is known to inhibit this enzyme. Some studies have suggested that green tea can improve cognition in these children, prompting some parents to start giving the affected children green tea extracts

as supplements in their diet. However, EGCG has not been approved for the treatment of cognitive disability in Down's syndrome. EGCG appear to have little effect after 3 years of age according to the study.⁴⁻⁶ The reported study had categorized 13 children in the following strands:

- a. Age 13-18: four children received green-tea extract for since late in adolescence.
- b. Age 4-12: two children for whom the report doesn't specify the age at which treatment began, but is presumably a few years.
- c. Age 0-3: seven children, four children had been receiving green-tea extract for since early in their development

According to this study, the 13 affected children were given EGCG. Six of the children who were given EGCG before the age of three had facial features that are same or matched for those children without the disorder. Previous study by the same researchers found out that young adults with the disorder who took EGCG for a year performed better in tests of memory and reasoning. The EGCG dose used in the study was equivalent to drinking eight cups of tea per day. According to reports, experiments in mouse model of Down's syndrome showed EGCG seem to, if administered early, improve skull, facial and limb development in these children.

There was about 30% less facial variation from non-DS (EU) kids in children 0-3 with Down syndrome who had been treated with EGCG according to Dierssen, et al.⁶

Advantages of the findings of this study if a human based equivalent gave a positive outcome:

- i. Minimising facial variation would reduce the social stigma associated with the disorder. However, there are ethical issues regarding whether the society should 'normalize' facial features of members of the society who look different.
- ii. Family attitudes vary too; some parents could in go all the way to give their children anything they thought could improve the facial and cognitive features of the disorder, even though they do not have any strong scientific evidence to back up their actions.
- iii. Others would not want to change a thing about their children with Down's syndrome.

Weakness of the study cited:

- a) The population studied was very small.
- b) There is no clear conclusions as children took the supplement for different lengths of time, thus large scale study is needed to get stronger conclusions and evidence, and optimum dose is needed to be determined because a study using mice suggested that very high amount of EGCG can cause severe facial and skeletal abnormalities.

Conclusion

It is not advisable for parents to give their affected children EGCG at this stage. However, this would understandably be hard for anxious parents as they have to wait for the outcomes of further longer-running clinical trials, and thus miss the opportunity to intervene at an early stage which would have been beneficial for their affected children. The Down's syndrome debate will surely continue for some time to come.

Acknowledgments

None.

Conflicts of interest

Authors did not report any potential conflicts of interests.

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