Temporal increase in the rate of Down syndrome livebirths to older mothers in New York State

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SUMMARY  In New York State exclusive of New York City the standardised rate of Down syndrome in livebirths to women 35 and over reported on birth certificates increased 30% in 1970 and later years, compared to the rate in 1965 and 1969. In contrast, there was no change in those under 35. A separate investigation revealed that selective temporal differences in reporting of cases born to older mothers did not account for the change. A similar increase in rates of cases born to older but not younger mothers in 1970 and later years has also been reported from Manitoba. These observations may be pertinent to apparent discrepancies between livebirth rates of Down syndrome and those reported at amniocentesis.

A recent study in Manitoba has reported almost a 70% increase in Down syndrome livebirths to mothers aged 35 and over but no change for those under 35 in the period 1970 to 1974 compared to 1965 to 1969. This finding prompted us to re-examine the data for livebirths in upstate New York (New York State exclusive of New York City). A significant trend, consistent with that in Manitoba although of smaller magnitude, occurred here and persisted in the years after 1974. There was, as in Manitoba, no evidence for a change in rate for younger mothers.

These inferences were derived from reports of Down syndrome or its synonyms on birth certificates of livebirths to residents of upstate New York, recorded in this jurisdiction, and from an investigation of the completeness of this source. For mothers 35 and over the reported rates per 1000 livebirths were 2.20 (186/84 727) in 1965 to 1969 and 2.74 (126/45 951) in 1970 to 1974 (p<0.001). Standardised rates, adjusted for the possible confounding effect of temporal trends in the numbers of livebirths by maternal age, were 2.17 and 2.81 per 1000 respectively, consistent with a 30% increase in maternal age specific rates. The reference population was upstate New York white livebirths in 1963 to 1974. The increase occurred in all three 5-year intervals between 35 and 49 and was of about the same magnitude for white and non-white populations.

For mothers under 35 the crude rates per 1000 were 0.31 (226/730 445) in 1965 to 1969 and 0.29 (191/655 848) in 1970 to 1974. The slight decrease of 6.5% is not significant ($\chi^2 = 0.4$; p ~ 0.60). The standardised rates were 0.32 and 0.30 per 1000, respectively.

The possibility of selective changes in reporting of Down syndrome upon birth certificates of older mothers was investigated. We determined the proportion of Down syndrome cases in birth certificates who had Down syndrome or a synonym recorded on their birth certificates. For mothers under 35 and over this proportion was 25/63 = 0.397 in 1965 to 1969 and 26/98 = 0.265 in 1970 to 1974. The decrease in completeness was not nominally significant ($\chi^2 = 3.0$; $0.10>p>0.05$) and the downward trend would, if anything, tend to obscure an increase in incidence in older mothers.

For mothers under 35 the completeness estimates for birth certificates were 31/89 = 0.348 in 1965 to 1969 and 61/199 = 0.307 in 1970 to 1974. This change was not significant ($\chi^2 = 0.5$; p ~ 0.45).

For 1975 and after, selective pregnancy termination was likely to lower livebirth rates of Down syndrome from levels that would have occurred in the absence of prenatal diagnosis. For mothers 35 and over the standardised rates for cases reported on birth certificates were 3.41, 2.46, and 2.17 for 1975, 1976, and 1977, respectively. After adjustment for
(a) the number of cases known to have been terminated, (b) estimates of the likelihood that an affected fetus would otherwise survive to livebirth, and (c) estimates of the likelihood that the affected livebirth would be reported on a certificate, the rates were 3·5, 2·7, and 2·6 per 1000, respectively. These may be underestimates because we are not likely to be aware of all affected pregnancies that were terminated. Nevertheless, these are greater than the rate of 2·17 per 1000 in 1965 to 1969. Thus, the trend to an increase over the 1965 to 1969 rates evidently persisted into 1975 and later years.

The trend in the Manitoba report for older mothers was significant at the 5% level, but no evaluation of the possibility of selective ascertainment of older mothers in later years was reported. The change was primarily confined to those aged 35 to 39.

In Montreal an increase in rate of about the same size as in New York State has also been noted for older mothers, although because of the paucity of data the trend is not formally significant. There was no change for younger mothers. In contrast, data for Australia and Jerusalem (kindly made available by S Harlap) show no evidence for any change.

It is emphasised that trends in those aged 35 and over are likely to be obscured if attention is confined only to changes in rates in the entire age span. In New York State, for example, the standardised rate of cases reported on birth certificates for mothers aged 15 to 49 rose only from 0·49 per 1000 in 1965 to 1969 to 0·54 per 1000 in 1970 to 1974.

These findings raise a question about the appropriateness of using rates in livebirths in earlier studies to project the current risk of a Down syndrome livebirth to women aged 35 and over, who have no known risk factor except advanced maternal age. A conservative approach, if any rate is to be quoted, would be to cite for any age a range between the earlier rate and a rate about 1·3-fold higher. The trend noted may partially explain the difference in rates between cases diagnosed in earlier years in livebirths and in recent years at amniocentesis, and in addition to late fetal deaths that would occur spontaneously after the usual time of prenatal diagnosis.

References


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