

# IMAGES

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## **Sex ratio imbalance in transposition of the great arteries and possible agricultural environmental risk factors**

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### **Abstract**

A significant bias in sex ratio has been documented for several congenital cardiac malformations. Transposition of the great arteries has been associated with a such a bias but no explanation has been proposed for this bias. We evaluated 95 isolated livebirths with transposition of the great arteries cases referred to the Sicilian Registry of Congenital Malformations from 1991 to 1998. We found a statistically significant male bias of 2.8 and this was significantly associated with both maternal and paternal occupational exposure to agricultural chemicals for male infants with transposition, but not for female infants. This study raises new questions about the possible role played by environmental chemicals in relationship to birth defects and to sex ratio imbalance.

**MeSH:** transposition of the great vessels, heart defects, congenital/epidemiology/etiology, neonatal diseases and abnormalities, sex ratio, risk factors, maternal exposure/adverse effects/statistics & numerical data, paternal exposure/adverse effects/statistics & numerical data, environmental exposure

### **Introduction**

Gender bias in different types of congenital defects is well know. A significant bias in sex ratio has been documented for congenital heart disease with several lesions occurring more frequently in males or in females.<sup>1,2</sup> This difference may be related to differences in hormonal constitution.

It has been proposed that foetal sex is partially determined by hormone levels of both parents around the time of conception has put forward<sup>3-5</sup> but it is unclear whether such hormonal variations may also be responsible for sex-biasing of congenital anomalies.

A literature search shows that transposition of the great arteries has been shown to have a gender bias (table 1) but no explanation has been put forward in order to account for this observation.

Table 1 Sex ratio of transposition of the great arteries in published reports

<b>Sex ratio</b>	<b>Reference</b>
3.22:1	6
3:1	7
2.8:1	Present study
2.30:1	1, 8
2.14:1	9
2.11:1	7
2.07:1	10
2:1	11, 12
1.67:1	13
1.56:1	14
1.50:1	15

In this study, we compare gender of patients with transposition with controls. In the general population, females tend to be smaller than male and in this study, we also attempt to relate gender ratios of patients with transposition with birth weight, maternal age and parental occupation.

## Methods

We evaluated 95 isolated livebirths with transposition of the great arteries cases referred to Sicilian Registry of Congenital Malformations from 1991 to 1998, and compared these with a control group of 1000 consecutive newborns from the same geographic origin. All types of transposition of the great arteries were evaluated together and we excluded cases with other associated birth defects.

Statistical analysis was done by  $\chi^2$  and Student's t-tests. Values of  $p < 0.05$  were considered significant.

## Results

We found a sex ratio (male/female) of 2.8 in transposition of the great arteries while the control group had a sex ratio of 1.04. This difference was statistically significant ( $p < 0.001$ ).

We did not find any statistical association between birth weights and gender bias in transposition of the great arteries and controls.

Stratification of our cases by gender and maternal age was not significant, with a mean maternal age of 29 years for both male and female cases of transposition of the great arteries ( $p = 1$ ).

A statistically significant association both for maternal ( $p = 0.03$ ) and paternal ( $p = 0.04$ ) occupation related to agriculture was found for males with transposition, while none was found for affected females.

## Discussion

Transposition of the great arteries occurs more commonly in males than in females. Moreover, in transposition of the great arteries, gender and birth weight are independent factors.

Hytten and Leitch<sup>16</sup> proposed that a high male sex ratio correlated with high maternal age, but James and Rostron<sup>17</sup> in a large sample of data found a decline in sex ratio of births at high maternal age. We did not find such an association in our study group.

Recently Loffredo et al<sup>18</sup> reported an association between transposition of the great arteries and maternal exposure to herbicides and rodenticides. Our findings support this hypothesis. The aetiological agent/s may be chemicals used in agriculture that produce a hormonal disruptor effect.

## Conclusion

The results of the present study, despite the limitations attributable to the small number of sample and controls, suggest further studies on environmental agents and their possible teratogenic effect.

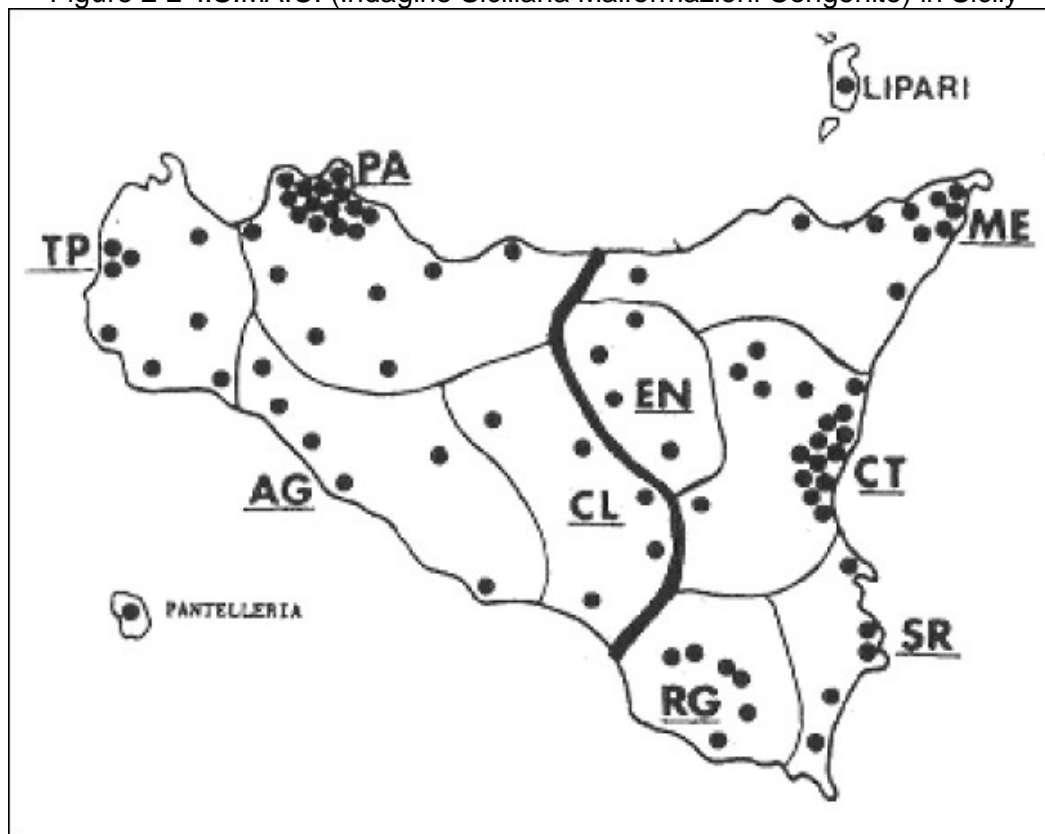
## Related link

Italian Congenital Malformation Registries  
<http://www.asmac.it/registriitaliani.html>

Figure 1 Regional congenital malformation registers in Italy



Figure 2 L' I.S.M.A.C. (Indagine Siciliana Malformazioni Congenite) in Sicily



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