Isolated esophageal atresia and perinatal risk factors

S. Bianca, G. Ettore
1Registro Siciliano Malformazioni Congenite (ISMAC), Dipartimento di Pediatria, 2Dottorato di Ricerca in Malattie Genetiche dell’Età Evolutiva, Università di Catania, and 3Divisione di Ostetricia e Ginecologia, Azienda Ospedaliera “Garibaldi”, Catania, Italy

SUMMARY. Esophageal atresia (EA) is a relatively rare alimentary tract congenital anomaly. We studied perinatal risk factors of 90 live birth cases of isolated EA with (40 cases) or without (50 cases) tracheal fistula. We found sex ratios of 1.43 for total EA cases and 1.5 for both subgroups of EA with or without tracheal fistula. Evaluation of parity showed statistically significant values for low parity and for high multiparity for EA with and without tracheal fistula. Birth weight evaluation revealed statistically significant values for both subgroups. We did not find statistical significance both for maternal age and gestational age. The etiology of esophageal atresia is complex and heterogeneous and within each subgroup, apparently different etiologies may exist, resulting in differences in epidemiologic characteristics. Moreover, some causes linked to genetics and gene–environment interaction may be involved. We think that parity and low birth weight can be considered as risk factors for EA, and an accurate evaluation of reproductive history can be useful for the provision of genetic and perinatal counseling.

INTRODUCTION

Esophageal atresia (EA) is a relatively rare alimentary tract congenital anomaly characterized by absence of continuity or narrowing of the esophagus, with or without tracheal fistula. The stated prevalence at birth of this condition varies according to different studies, but figures of around three per 10 000 births are often quoted. It is a heterogeneous entity and different anatomic forms are described both with and without fistula. Moreover, it is not certain that these variants all represent the same etiologic and pathogenetic entity. With exception of the cases where EA is part of a chromosomal or of a known monogenic or teratogenic syndrome, the etiology fit into a multifactorial model. A number of epidemiologic studies have been published on esophageal atresia searching for possible etiologic factors but, up to now, no definitive explanation has been made. Prompted to literature observations, we studied perinatal risk factors of our affected cases.

MATERIALS AND METHODS

We evaluated 90 live birth cases of isolated EA, with (40 cases) or without (50 cases) tracheal fistula, referred to the Sicilian Registry of Congenital Malformations database (study period 1991–98). A sample of 2000 consecutive healthy newborns with the same geographic origin was used as control group. For each case and for each control, data on maternal age, gestational age, parity, and previous pregnancy was available. All data were collected by a questionnaire interview administered by medical doctors and no recall bias was present. Statistical analysis was performed by \( \chi^2 \)-test and Student’s \( t \)-test. Values of \( P < 0.05 \) were significant.

RESULTS

It has been suggested that EA presents with a sex ratio (male/female) imbalance, we evaluated our data and we found sex ratios of 1.43 for total EA cases and 1.5 for both subgroups of EA with or without tracheal fistula. These values are not statistically significant but are higher than the population sex ratio of 1.06 and than that reported, 1.25. Maternal age was not statistically significant for all groups with an average maternal age of 28 ± 5.8 years.
When we evaluated the maternal reproductive history for previous spontaneous abortions, we found no statistically significant values for all conditions. Evaluation of parity showed statistically significant values for parity 1 (one previous pregnancy before affected newborn) for EA with tracheal fistula \((P = 0.03)\) and for EA without fistula \((P = 0.02)\). We also found statistically significant values for high multiparity (≥3 previous pregnancies before affected newborn) both for EA with fistula \((P = 0.04)\) and without fistula \((P = 0.03)\). If we stratified our data both for maternal age and low parity, we found a statistical significance for women older than 35 years \((P = 0.001)\).

The evaluation of gestational age and birth weight revealed no significance for gestational age and statistically significant values for all cases \((P = 0.01)\) and both for EA with \((P = 0.005)\) and without \((P = 0.002)\) fistula. Prompted by sex ratio imbalance evidence, we stratified the birth weight for sex and we found significant values for all subgroups.

**DISCUSSION**

There is still much to learn about factors that affect pregnancy outcome and the way in which they interact. An association between esophageal atresia and fertility problems has been suggested previously,\(^1,2\) with an increased risk at low parity, which could be the results of an indirect effect of a fertility problem. Moreover, a small effect of maternal age and parity has also been described previously, with a reported excess in women over 35 years.\(^3,4\) Our study confirms these results and adds an effect of multiparity as risk factor for EA. Between birth parameters, we found an association with low birth weight independently of gestational age, which shows a possible prenatal intrauterine growth retardation.

Esophageal atresia is probably a heterogeneous entity with some gene–environment implications in its etiology, and the reproductive history of EA mothers can be helpful to search for etiologic factors. Genetic hypothesis cannot be ruled out and only better knowledge of the genetic mechanisms involved in EA etiology will explain the epidemiologic associations.

**CONCLUSIONS**

Epidemiologic differences between defects, and between types within defects, may reflect differences in timing of the pathologic process or differences in susceptibilities, and emphasize the need to evaluate each defect and its types separately in epidemiologic studies.\(^5\)

The etiology of esophageal atresia is complex and heterogeneous and within each subgroup, apparently different etiologies may exist, resulting in differences in epidemiologic characteristics. Moreover, some causes linked to genetics and gene–environment interaction may be involved, although there is still a lot to do, especially in clarifying the role of genetics in producing susceptibility to the environment. We think that parity and low birth weight, can be considered as risk factors for EA, and an accurate evaluation of reproductive history can be useful in the provision of genetic and perinatal counseling.

**References**