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ANAL ATRESIA: EFFECT OF SMOKING AND DRINKING HABITS DURING PREGNANCY

Ping YUAN,[1,2] Isao OKAZAKI,[2] and Yoshikazu KUROKI[1,*]

[1]*Division of Medical Genetics, Kanagawa Children's Medical Center, 2–138–4 Mutsukawa, Minami-ku, Yokohama 232, Japan*
[2]*Department of Community Health, Division of Community Health and Environmental Medicine, School of Medicine, Tokai University, Bohseidai, Isehara, Kanagawa 259–11, Japan*

Summary Using data compiled from 216,707 births from the population-based Kanagawa Birth Defects Monitoring Program (KAMP), we conducted a case-control study to evaluate the effect of maternal smoking and/or drinking during pregnancy on the risk of infants' anal atresia in 1989–1994. The frequency of maternal smoking (including passive smoking) and/or maternal drinking during pregnancy among 84 infants with anal atresia was compared with 174 matched controls. The 84 anal atresias include 49 cases of isolated anal atresia and 35 cases of syndromal anal atresia. Our findings suggest that maternal drinking during early pregnancy is associated with an increased risk of isolated anal atresia (OR=4.8, 95% CI 1.2 to 19.1, $p<0.05$). A slightly increased trend was also observed in the association of maternal smoking during pregnancy with both in the pooled groups of anal atresia (OR = 1.4, 95% CI 0.5 to 3.6).
Key Words anal atresia, drinking, smoking, case-control study, birth defects monitoring

INTRODUCTION

Anal atresia is a common congenital anomaly in the newborn babies observed at a rate of 1 in 2,500 to 5,000 live births (Anderson and Reed, 1954; Stephens and Smith, 1971; Nagashima, 1994). The majority of reported cases of anal atresia were not familial (Oeconomopoulos, 1961; Stephens and Smith, 1971), while others have described that anal atresia could be a hereditary disease. It has been suggested that the anomaly could be caused by an autosomal dominant, autosomal recessive or sex-linked gene (Weinstein, 1965; Saeki and Akiyama, 1978; Schwoebel

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* To whom correspondence should be addressed.

et al., 1984; Nagashima, 1994). However, the clinician has an impression that smoking and/or drinking habits of patients' mothers during pregnancy could elevate the risk of anal atresia.

Anal atresia can be divided into two groups: one accompanied by multiple malformations with or without recognized chromosomal abnormalities, and the other having no other malformations. The former is called syndromal anal atresia, and the latter is called isolated anal atresia by the present authors. Isolated anal atresia has been considered not due to primary chromosomal abnormalities of germ cell, but rather is caused by several intrauterine environmental factors that affect growth and development of embryos. Of these environmental factors, tobacco and alcohol have been reported to influence the development of fetus. Therefore, we studied the effect of smoking and drinking during pregnancy on isolated anal atresia and syndromal anal atresia in order to clarify their etiological implications of an intrauterine environment.

We report here the results of a population-based case-control study of anal atresia and maternal lifestyles, such as smoking (either active or passive) and drinking habits during pregnancy, using the data from the KAMP.

SUBJECTS AND METHODS

Ninety-four cases with anal atresia were ascertained from 216, 707 single births, including stillbirths, born in Kanagawa Prefecture, during the period between April 1989 and March 1994. Sixty cases were males, 28 were females, and 6 were undermined. Fifty-three cases (56.4%) had anal atresia without other malformations (isolated anal atresia). Seven cases with recognized chromosomal syndromes and 34 cases with multiple malformations combined representing syndromal anal atresia (43.6%). In both groups, 14 cases were stillborn, and 6 died within 7 days after birth; 16 cases were diagnosed prenatally.

In the KAMP, all malformed cases are as well as all multiple births are registered with two consecutive normal control infants. Therefore, controls are twice in number of malformed cases. In this study, two controls for each anal atresia case were selected from the control populations. They were matched in respect to maternal age groups (5-years interval), sex, parity, and season of birth. Parental smoking habits, periods of smoking (first, second, and third trimester), and the amount of cigarettes smoked were studied. Maternal drinking habit, periods of drinking during pregnancies and the amount of alcohol consumption were also studied. Ten cases and 14 controls were excluded from this study because of unreliable data concerning smoking and alcohol consumption. Therefore, final number of cases and controls was 84 and 174, respectively.

Parental occupations were not considered in this study because 97% of the parents of both the cases and controls had not been reported about any exposure of specific chemicals or physical factors at work.

Statistical analysis was performed using High-quality Analysis Libraries for Business and Academic Users' [HALBAU] program. The criterion of significance was taken as $p<0.05$. Association between anal atresia and smoking and/or alcohol was estimated by odds ratios (OR) with 95% confidence intervals.

RESULTS

Some vital data of anal atresia are shown in Table 1. The gestational age and weight at birth were lower than those in the KAMP ($p<0.001$, $p<0.001$).

Table 2 shows the comparison of background data of the mothers of infants with anal atresia with the mothers of normal infants. The history of previous

Table 1. Vital information of the infants with anal atresia, Kanagawa, Japan, 1989–1994.

Characteristics of infants with anal atresia	Isolated n=49 (%)	Syndromal n=35 (%)	Total n=84 (%)
Mean maternal age (yr)[a]	28.7±4.7	29.6±5.2	29.1±4.9
Mean paternal age (yr)[b]	32.7±5.4	32.1±5.6	32.1±5.6
Sex			
male	38 (77.6)	18 (54.3)	57 (67.9)
female	11 (22.4)	12 (34.3)	23 (27.3)
undetermined	0	4 (11.4)	4 (4.8)
1st live births	23 (46.9)	17 (48.6)	40 (47.6)
2nd or over live births	26 (53.1)	18 (51.4)	44 (52.4)
Live births	47 (95.9)	21 (60.0)	68 (81.0)
Death within 7 days after birth	0	5 (14.3)	5 (6.0)
Stillborns	2 (4.1)	9 (25.7)	11 (13.1)
Mean gestational age (w)[c]	37.9±2.9	34.8±4.3	36.6±3.9
Mean birth weight (g)[d]	2,851.9±615.5	1,930.9±760.6	2,468.2±817.5
Period of diagnosis			
prenatal	2 (4.1)	13 (37.1)	15 (17.9)
postnatal	47 (95.9)	22 (62.9)	69 (82.1)
Anal atresia found in			
known syndromes	—	18 (51.4)	—
unspecified MCA*	—	17 (48.6)	—

[a] It showed no difference from those in the KAMP population (mean 29.7 years).
[b] It showed no difference from those in the KAMP population (mean 32.8 years).
[c] It was shorter than the mean gestational week in KAMP (38 w±1 w) during the same period ($p<0.001$).
[d] It was lower than the mean birth weight in KAMP (3,070 g±437 g) during the same period ($p<0.001$).
* Multiple congenital anomalies.

births with malformations was more common in the cases (3.6%) than controls (none), although this difference was not statistically significant.

Numbers of infant with anal atresia by smoking and/or drinking of the parents are shown in Table 3. About 10.7% of the mothers of infants with anal atresia and 8.0% of the mothers of controls were smokers without drinking, and the rate of drinker without smoking during pregnancy was 13.1% and 8.5%, respectively. In isolated anal atresia, mothers who smoked or drank were more numerous (12.2%, 14.3%), compared with the controls (8.0%, 8.5%). However, these differences were not statistically significant. The prevalence of mothers habit of both smoking and drinking during pregnancy was similar between cases and controls (2.4% *vs.* 2 3%).

Table 2. Comparison of the background between the mothers of infants with anal atresia and the mothers of normal control infants.

Characteristics	Anal atresia n=84 (%)	Controls n=176 (%)	OR[a] (95% CI[b])
Consanguineous marriage	0	0	
History of			
spontaneous abortions	8(9.5)	26(14.8)	0.6(0.2-1.5)
stillborns	0	4(2.3)	—
delivering births with malformations	3(3.6)	0	—
exposure to high level radiation	0	1(0.6)	—
During early pregnancy			
any abnormality	6(7.1)	18(10.2)	0.7(0.2-1.9)
drugs used	10(11.9)	18(10.2)	1.2(0.5-2.9)
exposure to radiation	1(1.2)	3(1.7)	0.7(0-7.7)

[a] Odds ratio. [b] 95% confidence intervals.

Table 3. Number of cases of anal atresia by smoking and/or drinking parents.

Smoking		Mother's drinking	Isolated n=49 (%)	Syndromal n=35 (%)	Total n=84 (%)	Controls n=176 (%)
Mother	Father					
−	−	−	17(34.7)	14(40.0)	31(36.9)	80(45.4)
+	−	−	0	0	0	1(0.6)
−	−	+	6(12.2)*	1(2.9)	7(8.3)	5(2.8)
+	−	+	0	0	0	1(0.6)
−	+	−	19(38.8)	12(34.2)	31(36.9)	63(35.8)
+	+	−	6(12.2)	3(8.6)	9(10.7)	13(7.4)
−	+	+	1(2.1)	3(8.6)	4(4.8)	10(5.7)
+	+	+	0	2(5.7)	2(2.4)	3(1.7)

* Statistically significant ($p<0.05$).

There were no cases and only 1 control mother who smoked during pregnancy but whose husband did not smoke. The mothers who drank during pregnancy but whose husband did not smoke were more numerous in the cases (8.3%) than in controls (2.8%). Such tendency was evident especially among isolated anal atresia group (12.2%) ($p<0.05$), showing an odds ratio of 4.8 (95% confidence intervals, 1.2–19.1). The frequency of passive smoking, with or without drinking during pregnancy, was 36.9% in the cases and 35.8% in the controls.

Smoker mothers during pregnancy with smoker husband (10.7%), as well as smoking and drinking with smoker husband (2.4%) were more prevalent among the cases compared to the controls (7.4%, 1.7%). The OR was 1.4 and 1.4, respectively. The result was not statistically significant. There was no difference about the frequency of both drinking habits and paternal smoking between the cases and controls.

Most mothers smoked less than 10 pieces of cigarettes per day in both cases and controls. Among the mothers who had drinking habit, 92.9% of cases and 100.0% of controls drunk small amounts. About a half of smoking husbands smoked 10–19 pieces of cigarettes per day both in cases and controls. Neither the levels of maternal smoking and alcohol consumption per day during pregnancy nor the level of husbands' smoking per day differed between cases and controls. The numbers of mothers who smoked throughout pregnancy (>28th week) were slightly more in cases than in controls.

DISCUSSION

Congenital anomalies are the most prevalent cause of infant deaths in Japan. Some recent epidemiological studies have clarified that maternal lifestyles, such as smoking or drinking habits and passive smoking during pregnancy, provoke some congenital anomalies (Jones and Smith, 1973; Himmelberger *et al.*, 1978; Ericson *et al.*, 1979; Kuroki, 1988; Jacobson *et al.*, 1993; Yuan *et al.*, 1994), although there are negative reports (Borlee *et al.*, 1978; Marbury *et al.*, 1983; Pradat, 1992). However, to our knowledge, an association of anal atresia with smoking and/or drinking during pregnancy has not been previously reported. Our findings suggest that maternal drinking during early pregnancy elevated the risk of anal atresia, especially isolated anal atresia. Further studies are necessary to elucidate whether the increased risk of anal atresia is due to a teratogenic effect of alcohol or whether other confounding factors are present in combination with antenatal alcohol exposure.

A slightly increased trend was observed in the association of maternal smoking during pregnancy with isolated and syndromal anal atresia. It is important to analyze the combined and isolated effects of smoking and drinking habits on anal atresia. Further investigation is necessary to identify a dose effect of maternal drinking on infant anal atresia among their babies.

In recent studies, passive smoking has been considered to posses same effects on the fetus as active smoking (Martin and Bracken, 1986; Mathai *et al.*, 1992). Our results do not support the possibility that smoking by the husband, in the absence of maternal smoking and/or drinking during pregnancy, increases the risk of having infants with both groups of anal atresia. This can be explained by the fact that sample size is too small to explain the association, and the husbands may reduce smoking during pregnancy in this population.

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