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Maternal risk factors in cleft lip and palate: case control study

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SUMMARY. **Three hundred and six mothers who gave birth to babies with cleft lip, or palate, or both, were matched with 306 who gave birth to healthy babies in the same area during the same time period. Significantly more babies in the cleft group had a family history of clefts (48/306 compared with 7/306, *P*<0.0001). In the cases studied, combined cleft lip and palate was significantly more common among boys (82/157 compared with 57/149, *P*=0.02) and cleft palate alone among girls (48/149 compared with 22/157, *P*=0.0002). Significantly more mothers reported some sort of illness during early pregnancy (101/306 compared with 74/306, *P* = 0.02). There were no differences between the groups as far as dietary preferences were concerned but during early pregnancy the mothers who gave birth to babies with defects tended to drink less alcohol (<1 unit/week) (236 compared with 199, *P* = 0.001) and less coffee (<1 cup/week) (159/306 compared with 131, *P* = 0.03). However, in each case similar proportions gave up once the pregnancy was confirmed. Large multicentre studies are required to confirm or refute these findings.**

INTRODUCTION

Both hereditary and environmental factors have been implicated in the development of cleft lip, or palate, or both.[1] We have previously reported an epidemiological case control study in which we found that pregnant mother's dietary preference for green vegetables and dairy products might have some effect on incidence of clefts.[2–4] In the present paper, we report further results from the same study.

SUBJECTS AND METHODS

A total of 306 mothers who gave birth to babies with cleft lip, palate, or both, were matched with 306 who gave birth to babies without defects in the same district during the same time period. There were 157 boys and 149 girls in each group; the mean (SD) weight of the boys with clefts was 3079.5 (601.8) g and of the girls 3001.5 (664.7) g. The corresponding weights in the control group were 3144.3(537.0) g and 3063.0(563.3) g. The children with clefts were operated on at the Second

Table 1 – Family history of cleft lip, or palate, or both (*n* = 306 in each group). Figures are number (%) of families

	Cases	Controls
None	258(84)	299(98)*
History of cleft lip and/or palate	47(15.4%)	5(1.6%)
No answer	1(0.3%)	2(0.7%)
Total	306(100.0%)	306(100.0%)

*P<0.0001

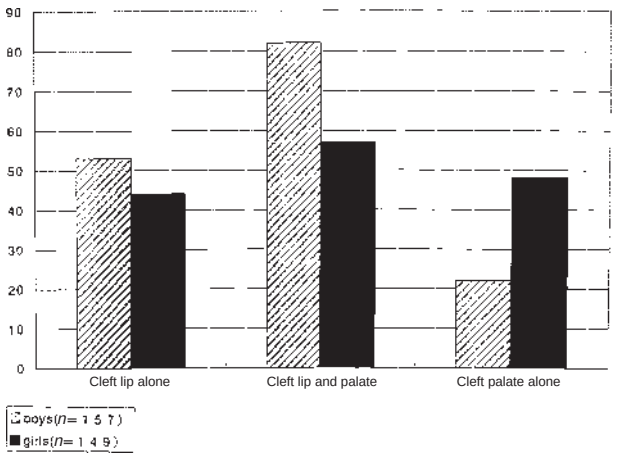

Fig. 1 – Types of cleft seen in the study. (*P = 0.46; **P = 0.02; and +P = 0.0002).

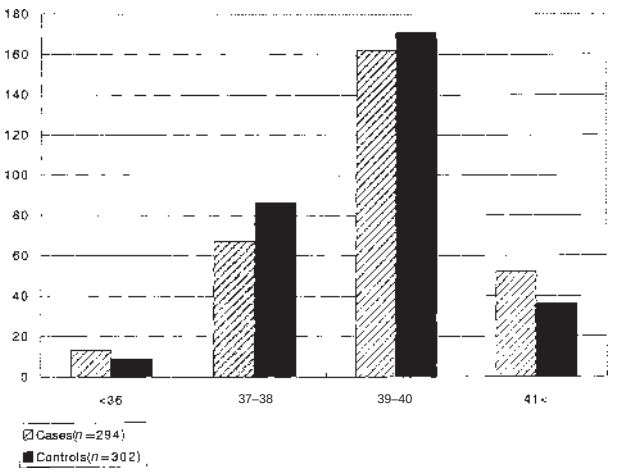

Fig. 2 – Weeks of gestation. Information was not given for 12 cases and four controls.

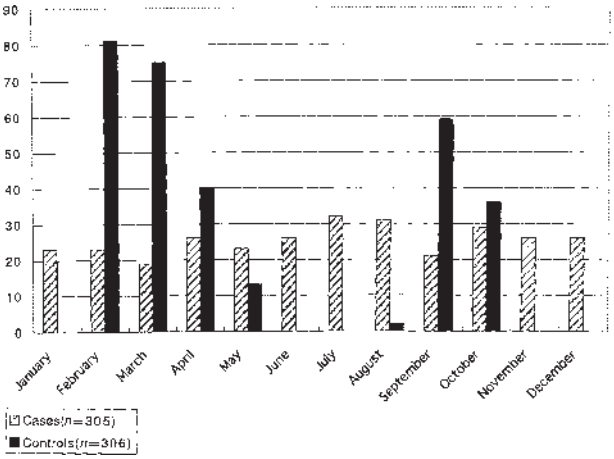

Fig. 3 – Month of birth. Information was not given for one of the cases.

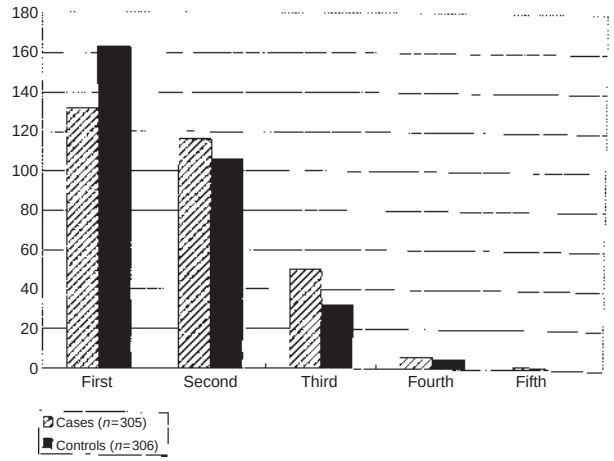

Fig. 4 – Order of birth among siblings. Information was not given for one of the cases.

Table 2 – Diseases reported by mothers during early pregnancy (n=306 in each group). Figures are number (%) of mothers

	Cases	Controls
None	205(67)	232(76)*
Influenza	2(1)	1(0.3)
Cold	66(22)	60(20)
Rubella	0	1(0.3)
Other	29(9)	7(2)
No answer	14(5)	7(2)

No mother developed measles, mumps, or chicken pox. *P=0.02

Department of Oral Surgery, Aichi Gakuin University, Nagoya, Japan. The control babies were followed up at four health centers in Nagoya, and parents gave their informed consent to the study. The following details were recorded about each baby: sex, date of birth, birth weight, order of birth among siblings, duration of gestation, and whether there was a history of congenital diseases and if so, of what.

We asked each mother her age at the time of delivery; her weight before pregnancy; her height, blood group, and occupation during early pregnancy; and what time she realized she was pregnant; how and when she changed her lifestyle during pregnancy (including details of alcohol and coffee consumption and dietary preferences).

Finally, we enquired whether there was a family history of consanguinity or cleft lip or palate.

Table 3 – Dietary preferences of mothers (306 in each group) Figures are number (%) of mothers

	Cases	Controls
Vegetables		
Like	286(93)	284(93)
Dislike	18(6)	20(7)
No answer	2(1)	2(1)
Fried food		
Like	272(89)	274(90)
Dislike	33(11)	31(10)
No answer	1(0.3)	1(0.3)
Seasoning used		
Light	155(51)	168(56)
High	150(49)	138(45)
No answer	1(0.3)	0
Foods eaten more than 5 times a week		
Meat	144(47)	141(46)
Dairy product	197(64)	222(73)
Confectionery	40(13)	40(13)

STATISTICAL ANALYSIS

The differences between groups were assessed with Fisher's exact test and the χ^2 test with Yates' correction, as appropriate.

RESULTS

There were no significant differences in mother's age at delivery, body mass index (BMI=weight(kg) divided by height(m)^2), occupation during early pregnancy, or blood group (data not shown).

Types of cleft and family history of cleft disease are shown in Table 1 and Figure 1. Significantly more babies among the cases gave a family history of clefts (48/306 compared with 7/306, P<0.0001). In the series of cases presented, combined cleft lip and palate was significantly more common among boys (82/157 compared with 57/149, P=0.02), and cleft palate alone among girls (48/149 compared with 22/157, P=0.0002), but there was no difference between the sexes in the incidence of cleft lip alone (Fig. 1). Weeks of gestation did not differ between the groups (Fig.2). Months of birth varied considerably between the groups, but showed no consistent pattern (Fig. 3). Order of birth among siblings was similar in the two groups (Fig. 4).

Significantly more mothers reported some sort of illness during early pregnancy among the cases than among the controls (101/306 compared with 74/306, P=0.02) but the subgroups were too small to submit to statistical analysis (Table 2).

Table 4 – Changes in alcohol and coffee consumption as a result of pregnancy. Figures are number (%) of mothers

	Cases before	(*n*=306) During	Controls before	(*n*=306) During
Alcohol				
No. of units/week:				
< 1	236(77)*	274(90)	199(65)*	261(85)
1–2	40(13)	20(7)	53(17)	31(10)
3–4	13(4)	1(0.3)	27(9)	7(2)
5–6	8(3)	2(1)	23(8)	3(1)
No answer	9(3)	9(3)	4(1)	4(1)
Amount drunk by spouse				
None	105(34)	–	75(25)	–
1–2	47(15)	–	52(17)	–
3–4	42(14)	–	33(11)	–
5–6	109(36)	–	142(46)	–
No answer	3(1)	–	4(1)	–
Coffee				
No. of cups/week				
< 1	159(52)†	183(60)	131(43)†	165(54)
1–2	126(41)	110(36)	141(46)	129(42)
3–4	14(5)	9(3)	24(8)	7(2)
5–6	3(1)	0	6(2)	2(1)
No answer	4(1)	4(1)	4(1)	3(1)

*P=0.001; † P=0.03

There were no differences between the groups as far as dietary preferences were concerned (Table 3). Interestingly, the mothers who gave birth to babies with defects tended to drink less alcohol (<1 unit/week) before pregnancy than control mothers (236/306 compared with 199/306, P<0.001), but similar proportions reduced their drinking or gave up after they had found out that they were pregnant (Table 4). They also drank less coffee (159/306 drank less than one cup/week compared with 131/306, P=0.03, Table 4), but again similar proportions gave up.

DISCUSSION

These results have shown several significant differences in general terms between the groups, but because the subgroups were so small it was not possible to identify which particular factors were responsible. Larger studies will be needed to confirm or refute experimental work published elsewhere.[5–7]

To confirm whether the results of this survey are peculiar to the area around Nagoya, we plan a nationwide multicentre study of 13 university hospitals. We would also like to take part in joint research with hospitals in other parts of the world.

Acknowledgements

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