Introduction

In the fall of 2008 in China, an unprecedented epidemic of urinary stones that affected infants and children after the consumption of melamine-tainted milk powder was reported. Totally, 294,000 infants and children had been diagnosed to have urinary stones by the end of November 2008. More than 50,000 infants and children had been hospitalized and six deaths were confirmed (1). Although more than half of melamine-related urinary stones cases recovered after a short hospital stay, many infants and children still had residual stones at the time of discharge (2). Thus, effects of melamine continue to raise concerns for public health in China and probably in other countries all over the world.

Since the outbreak of melamine-related urinary stones in infants and children, a series of studies have been published concerning the diagnosis, clinical symptoms and treatments of urinary stones, and many epidemiologic investigations are also carried out to explore and identify the features and risk factors, such as gender, age, birth type, urinary malformation, melamine concentration, positive family history and urinary pH. Gansu Province locating in the northwest of China has low socioeconomic conditions and large population. During this outbreak of urinary stones caused by melamine, Gansu Province is a heavily affected area (3). A case-control study was performed among 190 infants to explore new influencing factors. 35 objects (aged 12.8 ± 5.0

Abstract
Melamine is a new risk of urinary stones. Gansu province is a heavily affected area and has large population and underdeveloped economy. We hypothesized that number of family members and family income may play significant roles in the formation of urinary stones. A case-control study was performed among 190 infants. Results showed that the case group had less numbers of family members than the control (4.4 vs. 5.6, respectively). The multivariate logistic regression analysis indicated that number of family members was an independent influencing factor associated with urinary stones (OR, 0.606; 95% CI, 0.411-0.893; P = 0.011). Family income, however, did not exhibit a significant difference. Observed results suggested that number of family members was a new and significant influencing factor to affect the risk of melamine-associated urinary stones.

Keywords: Family, Melamine, Urine
months, 25 boys and 10 girls) were diagnosed with urinary stones and constituted the case group; 155 (aged 12.4 ± 4.2 months, 99 boys and 56 girls) did not have urinary stones and constituted the control group.

**General characteristics and feeding conditions**

In general characteristics, there were no significant differences in age, sex, birth weight, family income, etc. between the case and control group ($P > 0.05$). The factor—number of family members, however, exhibited a significant difference ($P = 0.006$), and the average numbers of family members in the case and control group were 4.4 and 5.6, respectively. In feeding conditions, feeding melamine-tainted milk powder and cumulant of exposure showed significant differences. In the case group, 82.9% study subjects were fed with milk powder contaminated by melamine, but only 56.8% infants and children in the control group suffered from the melamine-tainted milk powder ($P = 0.004$). Furthermore, as compared to the control group, the case group had more cumulant of exposure to melamine ($P = 0.006$) (Table 1).

### Table 1: Comparisons of general characteristics and feeding conditions

| Characteristics                                | Case group | Control group | $\chi^2$ | t value | $P$ value |
|------------------------------------------------|------------|---------------|---------|---------|-----------|
| Number of children                             | 35         | 155           |         |         |           |
| Age (months)                                   | 12.8 ± 5.0 | 12.4 ± 4.2    | 0.516   | 0.607   |           |
| Sex (male, %)                                  | 25 (71.4)  | 99 (63.9)     | 0.719   | 0.396   |           |
| Birth weight (kg)                              | 3.1 ± 0.4  | 3.2 ± 0.5     | 1.118   | 0.265   |           |
| Birth type (preterm, %)                        | 3 (8.6)    | 8 (5.2)       | 0.609   | 0.435   |           |
| Delivery way (eutocia/cesarean)                 | 33/2       | 147/8         | 0.018   | 0.895   |           |
| Father's age (years)                           | 28.9 ± 4.2 | 28.3 ± 4.0    | 0.759   | 0.449   |           |
| Father's educationa                            | 0/3/29/1/2 | 0/3/121/22/9 | 7.096   | 0.069   |           |
| Mother's age (years)                           | 26.5 ± 4.2 | 26.3 ± 4.3    | 0.168   | 0.867   |           |
| Mother's educationb                            | 0/5/29/1/0 | 2/12/128/7/6 | 3.360   | 0.500   |           |
| Number of family members                       | 4.4 ± 1.0  | 5.6 ± 1.2     | 2.802   | 0.006*  |           |
| Family income (Yuan/year)b                     | 33/2/0     | 138/16/1     | 0.953   | 0.621   |           |
| Place of residence (city/countryside)          | 1/34       | 4/151         | 0.009   | 0.926   |           |
| Feeding patterns (breast milk/formula/mixture, n) | 15/10/10 | 81/26/48     | 2.650   | 0.266   |           |
| Feeding melamine-tainted milk powder           | 29 (82.9)  | 88 (56.8)     | 8.210   | 0.004*  |           |
| Duration of exposure (months)                  | 7.8 ± 1.5  | 6.7 ± 2.2     | 1.081   | 0.282   |           |
| Cumulant of exposure (kg)                      | 15.6 ± 4.9 | 9.6 ± 3.2     | 2.773   | 0.006*  |           |
| Vitamin AD supplementation                     | 5 (14.3)   | 21 (13.5)     | 0.013   | 0.909   |           |
| Calcium supplementation                        | 26 (74.3)  | 121 (78.1)    | 0.233   | 0.629   |           |

*Note: a. The levels of education are illiteracy, primary, junior high school, High school and college; b. The levels of family income are "<10000", "10000-30000" and ">30000"; * $P < 0.05$, significantly different from the control group.

**Medical histories**

The medication history of infants and children had significant difference ($P = 0.031$). Infants and children in the case group received more medications than these in the control (60.0% vs. 40.7%). However, past medical history of urinary stones of infants and children, family history of urinary stones and medication history of mother during pregnancy did not exhibit significant differences ($P > 0.05$) (Table 2).
Table 2: Comparisons of medical histories between the case and control groups

| Contents                                      | Case group | Control group | χ²   | P value |
|----------------------------------------------|------------|---------------|------|---------|
| Past medical history of urinary stones of infants and children (yes, %) | 1 (2.9)    | 6 (3.9)       | 0.083| 0.774   |
| Medication history of infants and children (yes, %) | 21 (60.0)  | 63 (40.7)     | 4.642| 0.031*  |
| Family history of urinary stones (yes, %)    | 1 (2.9)    | 12 (7.7)      | 2.892| 0.717   |
| Medication history of mother during pregnancy (yes, %) | 5 (14.3)  | 25 (16.1)     | 0.073| 0.787   |

Note: * P < 0.05, significantly different from the control group.

Logistic regression analysis on independent influencing factors of urinary stones

The multivariate logistic regression was carried out to identify and assess significant independent risk factors associated with stones in urinary system. The dependent variable was the urinary stones; the independent variables included number of family members, medication history, feeding melamine-tainted milk powder and cumulant of exposure. The results indicated that OR of number of family members was 0.606 (95% CI, 0.411-0.893; P = 0.011); OR of feeding melamine-tainted milk powder was 3.380 (95% CI, 1.981-11.646; P = 0.040) (Table 3). Gansu Province was heavily affected by melamine-tainted milk powder. WHO recommends that a tolerable daily intake (TDI) for melamine is 0.2 mg/kg of body weight (1); however, the average melamine concentration in 52 Sanlu infant formula samples collected from Gansu province is 1674 mg/kg (3).

Table 3: The multivariate logistic regression analysis on independent influencing factors of urinary stones

| Variables                                      | β value | S.E.  | Wald  | P value | OR   | 95% CI       |
|-----------------------------------------------|---------|-------|-------|---------|------|--------------|
| Number of family members                      | -0.501  | 0.198 | 6.413 | 0.011*  | 0.606| 0.411-0.893  |
| Medication history                            | 0.092   | 0.095 | 0.935 | 0.333   | 1.096| 0.910-1.320  |
| Feeding melamine-tainted milk powder          | 1.218   | 0.631 | 3.722 | 0.040*  | 3.380| 1.981-11.646 |
| Cumulant of exposure                          | 0.040   | 0.022 | 3.521 | 0.061   | 1.041| 0.998-1.086  |

Note: * P < 0.05, significantly different from the control group.

Our findings demonstrated that exposure to melamine-contaminated milk powder would lead to the formation of urinary stones, and the number of family members would be a new and significant influencing factor, and more numbers of family members would protect infants and children from urinary stones. This association could be related to the exercise of infants and children. In a big family, infants and children have more chances and time to play with relatives, such as parents, brothers, sisters, etc. as compared to a small family. Through more exercise, on the one hand, the risk of stone formation in urinary system would be reduced; on the other hand, the formed stones could start moving down the urinary system quite a bit faster. It is reported that the augmented aerobic exercise in space may decrease the risk of stone formation in astronauts (4). Our current study has provided special insights into influencing factors associated with urinary stones, and the findings from this retrospective study would advance the understanding of the epidemiology of urinary stones related to melamine.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.
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The authors declare that there is no conflict of interest.

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