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Research

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Breastfeeding reduce the risk of Kawasaki disease in a Chinese population based case-control study

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Abstract

Background: Kawasaki disease (KD) is the leading cause of acquired heart disease in the pediatric age group in developed countries. But its etiology is unknown. We assessed whether breastfeeding time can influence risk of KD.

Methods: We collected feeding, clinical and laboratory details from 200 KD patients and 100 controls. Then we use SPSS to assess the comparison of the general characteristics of KD patients and control patients, and the Correlation of BF time with clinical and laboratory of KD patients.

Results: The haemoglobin level was significantly lower in Kawasaki disease patients compared with controls ($p < 0.05$). There were no significant differences between group of KD with coronary artery lesions (CALs) and group of KD without CALs in age, sex, WBC, platelet, HB,

CRP . However, there were significantly decreased frequencies for the longer breastfeeding time in KD patients without CALs when compared with KD patients with CALs (OR=668, 95%CI=0.454-0.984, p=0.041). Moreover, HB level were positively correlated with breastfeeding time in patients with KD (r=0.163, p=0.028)

Conclusion: We have shown that breast-feeding is associated with KD and the CALs. Breastfeeding may reduce the risk of KD with CALs. Breastfeeding may reduce the risk of KD with CALs.

Keywords: Kawasaki disease, breastfeeding, coronary artery lesions

Background

Kawasaki disease (KD) is a vasculitis of unknown etiology, which mainly occurs in infants and young children. The most severe complications that KD patients experience are coronary artery lesions (CALs), leading to myocardial ischemia, infarction and sudden death. At present, KD is the leading cause of acquired heart disease in the pediatric age group in developed countries[1].

Cause and pathogenesis of KD are unclear. Therefore literature is replete with multiple factors considered as associations of KD[2]. KD may occur with an aberrant immune response to some environmental trigger[3]. Recently researchers found that nutrition during critical windows in early life can influence and program later cardiometabolic health[4]. Breastfeeding is the best source of nutrition for infants to

optimize growth and development. The World Health Organization(WHO) recommends exclusive breastfeeding for the first 6 months of life, introduction of complementary foods at 6 months of age, and continued breastfeeding up to 2 years of age and beyond [5].

A Japanese study and a German study already have indicated a potential protective effect of breastfeeding in KD[6,7]. This suggested that breastfeeding potentially play a role in the pathogenesis of KD. But there are few study about the specific association between the breastfeeding and KD. Therefore, in a retrospective case-control study we investigated the association and impact of breastfeeding practices and on Laboratory indexes of KD.

Methods

This investigation was a retrospective analysis. All cases were performed at a single institution. The study was approved by the Ethics Committees of Chengdu women's and Children Central hospital. The medical records of all patients with a discharge diagnosis of KD admitted to the Chengdu Women's and Children's Central Hospital from September 2018 to September 2019 were retrospectively reviewed.

We collected 200 KD patients, as controls, 100 healthy children were selected.

We collected feeding, clinical and laboratory details from each KD case. All enrolled patients met the criteria proposed by the Japanese

Kawasaki Disease Research Committee[8]. Patients with KD were divided into 2 groups according to the presence of CAL: patients with CALs and patients without CALs. CALs were defined as a z score 2.5 in the right coronary artery or the left anterior descending coronary artery or the presence of ectasia or aneurysms. Coronary arterial lesion severity assessment was visualised using echocardiography or coronary artery angiography along with dilatation and/or evidence of ectasia and aneurysms. Collection of clinical data were approved by the Chengdu Women's and Children Central Hospital.

Statistical analyses

Statistical analysis was performed using SPSS version 20 software (SPSS Inc., Chicago, IL, USA). We presented the data as mean \pm standard deviation (SD) for all values. Statistical significance of the differences between the continuous variables was evaluated by One-way analysis of variance (ANOVA) or Kruskal – Wallis ANOVA and Mann – Whitney U tests. A Pearson's test was used to measure associations between sequential parameters. The association between breastfeeding time and Kawasaki disease risk was estimated by computing odds ratios and 95% confidence intervals from a multivariate logistic regression analysis. A *p* value of < 0.05 was considered to be statistically significant.

Results

As shown in Table 1, platelet count, white blood cell counts, C-reactive protein were higher in Kawasaki disease patients compared with controls ($p < 0.001$), whereas haemoglobin level was significantly lower in Kawasaki disease patients compared with controls ($p < 0.05$).

There were no significant differences between group of KD with CALs and group of KD without CALs in age, sex, WBC, platelet, HB, CRP (Table 2). However, there were significantly decreased frequencies for the longer breastfeeding time in KD patients without CALs when compared with KD patients with CALs (OR=668, 95%CI=0.454-0.984, $p=0.041$. Table2). Moreover, as shown in Table 3, HB level were positively correlated with breastfeeding time in patients with KD ($r=0.163$, $p=0.028$) (Table 3).

Discussion

It is widely accepted that breast-feeding has numerous health benefits for both the infant and mother[9] . Increasing evidence suggests that breast-feeding is associated with lower cardiovascular disease (CVD) risk factors [10].It is reported to be the most frequent pediatric systemic vasculitis globally, and the most important cause of acquired heart disease among children. There were only few studies about the association between breast-feeding and Kawasaki disease. Up to now, we are the first to report the relationship between breastfeeding and the KD laboratory index.

In addition to standard diagnostic criteria, KD patients may experience a variety of nonspecific clinical features, such as anemia[11]. Anemia is the most common clinical feature in KD patients and is thought to have a more prolonged duration of active inflammation[12]. Studies found that hemoglobin is a useful early differentiating feature between KD shock syndrome from toxic shock syndrome in a pediatric intensive care unit [13].

In this study, we showed that the HB level was significantly lower in Kawasaki disease patients, moreover, HB level was positively correlated with breastfeeding time in patients with KD. Therefore, we hypothesize that breastfeeding during early life may play a role in in the acute phase of KD.

Our analysis identified a statistically significant association between breastfeeding time and an reduced risk of CALs in KD children. It suggested that the longer breastfeeding time may play a protective factors in the development of KD CALs.

The authors observed protective effects of breastfeeding on the development of KD during the period from 6 to 30 months of age in the country in which KD is most common.

Among other advantages, breastfeeding seems to protect against a variety of infectious diseases [14] and non-breastfed children have a higher risk of developing allergies and bronchial asthma later in life [15].

During the perinatal and infancy periods, these and other factors potentially play a role in the pathogenesis of KD.

The WHO recommends that infants should be fed breast milk exclusively for the first six months of life. Our study provide further evidence for the promotion of breast-feeding. A large study from Japan has indicated that breastfeeding may be protective for KD[16], our data reinforce the findings.

Our study has limitations. The cross-sectional analysis cannot determine causality. Further, we were not able to adjust for unmeasured potential confounders, such as infant feeding patterns or early introduction of complementary foods. Another major limitation of this study was its relatively small sample size.

Conclusions

In summary, we have shown that breast-feeding is associated with KD and the CALs. The results from the present study add to the literature supporting a beneficial effect of breastfeeding on health-related parameters.

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Contributors Feifei Si conceptualised and designed the study, drafted the initial manuscript. Yanfeng Yang conducted analyses and reviewed and revised the manuscript for important intellectual content. Qian Duan contributed to interpretation of data and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all

aspects of the work.

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Availability of data and materials Please contact authors for data requests.

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