

Could maternal stress be a causal factor for nonsyndromic cleft lip and/or palate: A retrospective study

ABSTRACT

Background: The etiology of the nonsyndromic cleft lip and palate is multifactorial and not clearly defined.

Objective: To determine whether maternal stress could be a causal factor for the occurrence of nonsyndromic cleft lip and palate.

Materials and Methods: We conducted a retrospective observational study in which data from 50 mothers of children born with nonsyndromic cleft lip and palate and 50 mothers of noncleft children were analyzed. The outcomes defined were to study the association between the increased stress scores and the occurrence of nonsyndromic cleft lip and/or palate. Statistical analysis was performed using the Chi-square test.

Results: The association between the high maternal stress scores and the occurrence of nonsyndromic cleft lip and/or palate was not found to be significant ($P = 0.3220$). A significant association was noted between increased maternal age and increased stress levels in the cleft group ($P = 0.0001$).

Conclusion: No significant association was found between the increased stress scores and the occurrence of nonsyndromic cleft lip and/or palate. However, mothers of cleft children whose age was 35 years and above at the time of conception were noted to have higher stress levels.

Keywords: Cleft lip, cleft palate, maternal stress

INTRODUCTION

“Finding the cause is as equally important as the treatment.” The etiology of the nonsyndromic cleft lip and palate is multifactorial and not clearly defined to date. Various genetic, environmental, socioeconomic, and maternal health factors are considered responsible for the occurrence of nonsyndromic cleft lip and/or palate. Maternal stress is considered one of the etiological factors for the nonsyndromic cleft lip and/or palate. Elevated stress in pregnant mothers leading to increased cortisol levels and cytokine production is thought to play an important role in the alteration of the fetal blood flow. This eventually leads to oxidative damage at the cellular level and results in genetic alteration in the developing fetus.^[1]

Previous studies based on the association between maternal stress and the occurrence of nonsyndromic cleft lip and/or palate have been inconclusive. Some of them have supported the role of maternal stress as a contributory factor, while some

have denied it.^[2-7] We conducted this study with the objective of determining whether maternal stress could be a causal factor for the occurrence of nonsyndromic cleft lip and palate.

MATERIALS AND METHODS

We conducted a retrospective observational study over the period of 6 months, July 2018 to January 2019 at our tertiary care hospital. The data pertaining to the stress perceived during pregnancy were collected retrospectively from 50

KIRAN SUNIL MAHAPURE, RAJESH S. POWAR

Department of Plastic Surgery, KAHER's Jawaharlal Nehru Medical College, Belgaum, Karnataka, India


Address for correspondence: Dr. Kiran Sunil Mahapure, Department of Plastic Surgery, KAHER's Jawaharlal Nehru Medical College, Belgaum, Karnataka, India.
E-mail: drkiranmahapure@gmail.com

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mothers of children born with nonsyndromic cleft lip and/or palate coming to our cleft outpatient department for follow-up and similarly data from 50 mothers of children born with cleft lip and/or palate from the pediatric outpatient department.

Data collection

The inclusion criteria were as follows:

- Mothers of children <3 years old
- Mothers who agreed to give consent for the study.

The exclusion criteria are as follows:

- Mothers of children born with syndromic cleft lip and/or palate
- Mothers suffering from previous psychological conditions
- Mothers of children >3 years old.

The data were collected using the perceived stress scale tool,^[8] which consists of ten questions with five options to select the response from. The responses are never, almost never, sometimes, fairly often, and very often, rated between 0 and 4. The total score ranges between 0 and 40, scores <13 indicate low stress, scores between 13 and 26 indicate moderate stress, while scores >26 indicate high perceived stress. The perceived stress scale is a classic stress assessment instrument and was selected for the assessment after taking opinions from psychiatry consultants of our institution.

Data documentation

The filled questionnaires were reviewed by two reviewers independently, and disagreements were discussed among all reviewers and resolved via a consensus. Subsequently, the data were collected and tabulated using Microsoft Excel.

The study was informed and documented to the Institutional ethical committee but did not require ethical approval as this was an observational study and did not involve any intervention. The consent was obtained from the patients for their data collection. The nature of the study and the outcomes were explained to the patients. It was clearly explained to the participants that the data would be published only after removing the identification details and the data would be used for educational and research purposes.

Outcomes

The primary outcomes defined were to study the association of maternal stress with the occurrence of cleft lip and/or palate. The defined secondary outcome was to study the distribution of the levels of low, moderate, and high stress in both groups.

Statistical analysis

All outcomes were performed using the Chi-square test. The $P < 0.05$ was considered statistically significant.

RESULTS

Demographic characteristics

We analyzed data from a total of 100 mothers, 50 of children born with nonsyndromic cleft lip and/or palate, and 50 from children born without cleft lip and/or palate. Both groups were comparable in terms of maternal age and level of education. The mean age of the mothers in the cleft group was 28.14 years and that of the noncleft group was 29.34 years. The level of education of mothers of both groups is described in Figure 1.

Mean maternal stress scores

The mean stress scores in mothers of nonsyndromic cleft children were higher than those of mothers of noncleft children (17.58 ± 9.19 in the cleft group versus 15.52 ± 8.33) [Figure 2].

Distribution of stress levels

A significantly different distribution of stress levels was observed between the mothers of nonsyndromic cleft children and mothers of noncleft children. In the cleft group, 22% had high-stress scores, while 14% had high-stress scores in the noncleft group [Figure 3].

Statistical analysis

Association between maternal stress scores and the occurrence of cleft lip and/or palate

The association between the high maternal stress scores and the occurrence of nonsyndromic cleft lip and/or palate was not found to be significant ($P = 0.3220$, Chi-square = 2.2313).

Association between increased maternal age and increased stress levels

A significant association was noted between increased maternal age and increased stress levels in the cleft group ($P = 0.0001$, Chi-square = 54.8230) [Table 1 and Figure 4].

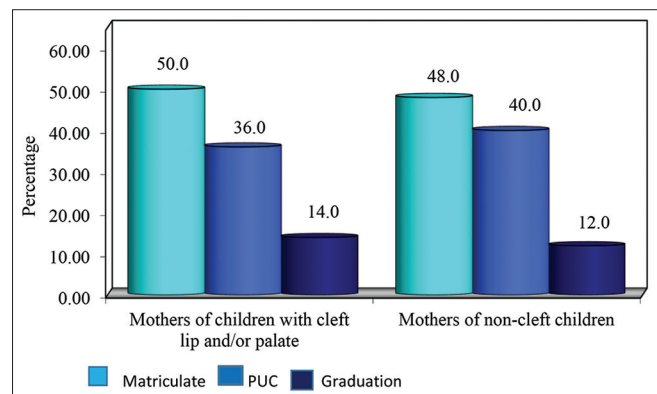


Figure 1: Level of education of the mothers

In the noncleft group, the association between increased maternal age and increased stress levels was not significant ($P = 0.3001$, Chi-square 7.230) [Table 2 and Figure 5].

To conclude, our study showed that the levels of stress were significantly associated with increased maternal age in mothers of nonsyndromic cleft children.

DISCUSSION

Increased maternal stress levels were thought to be the etiological factor for nonsyndromic cleft lip and/or palate by altering the fetal blood flow. Stressful life events elevate the maternal corticotrophin-releasing hormone and thus, the corticosteroid levels. Corticosteroids are proved to be teratogenic in animal models for various organ systems, neural tube defects. Furthermore, women who took corticosteroid medications during the first trimester of pregnancy were noted to have an increased risk of oral clefts.^[9] In low levels of stress or stress over a short duration, the physiology can still return to normal. It is the continuous high level of stress which possibly leads to abnormal development of cells.^[10]

Table 1: Association between increased maternal age with increased stress levels in the mothers of cleft children

Stress levels	Mild	Moderate	Severe	Total number of patients
Age of the mothers of cleft children				
20-24 yrs	16	0	0	16
25-29 yrs	4	14	2	20
30-34 yrs	0	5	5	10
>=35 yrs	0	0	4	4
Total	20	19	11	50

Chi-square=54.8230, * $P=0.0001$

Table 2: Association between increased maternal age with increased stress levels in mothers of non-cleft children

Stress levels	Mild	Moderate	Severe	Total number of patients
Age of the mothers of non-cleft children				
20-24 yrs	7	3	0	10
25-29 yrs	12	3	1	16
30-34 yrs	7	6	4	17
>=35 yrs	3	2	2	7
Total	29	14	7	50

Chi-square=7.230, $P=0.3001$

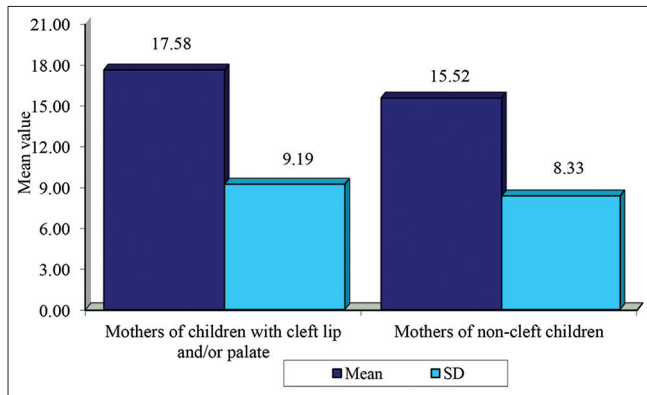


Figure 2: Comparison of the mean perceived stress scores between the two groups

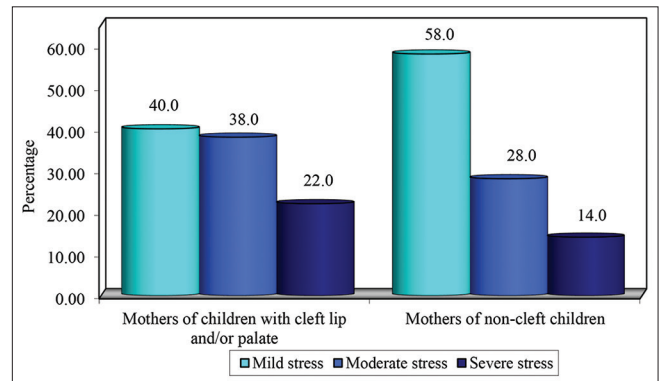


Figure 3: Distribution of stress levels within the groups

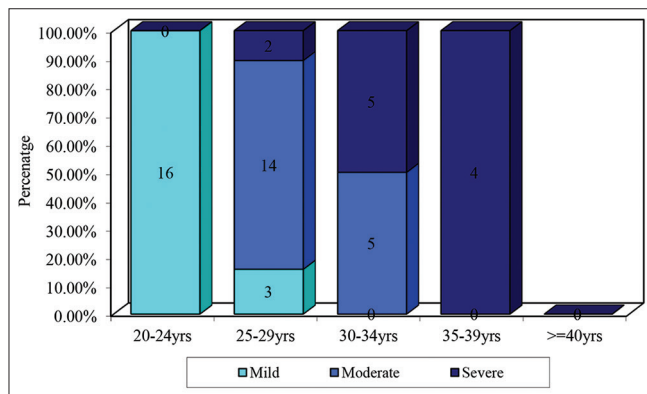


Figure 4: Association between age groups of mothers with stress levels in mothers of children born with cleft lip and/or palate

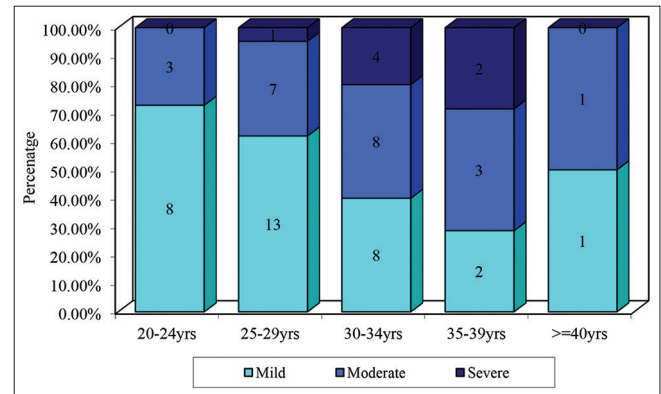


Figure 5: Association between age groups of mothers with stress levels in mothers of noncleft children

Several previous studies have assessed the association between various maternal factors and their association with the occurrence of nonsyndromic cleft lip and/or palate. Poradowska and Jaworska concluded in their study that 47.1% of mothers “were severely disturbed with depression and anxiety states.^[2] The incidence of clefts in 2003–2005 doubled than 1996–1998 in Basrah due to increased stress levels among the population, poor access to adequate nutrition, and environmental toxins, as stated by Fathallah.^[3] A study by Czeizel and Nagy supported the association between cleft palate and stress during the second trimester but no association for cleft lip,^[4] while Saxén concluded that both cleft palate and cleft lip are associated with stress during the second and third trimesters.^[5] The study done by Montenegro in Chile observed that there was an increased incidence of facial clefts in infants who were at the appropriate period during a major Earthquake in Chile, indicating the role of increased stress levels in the etiology of cleft lip and/or palate.^[6] Surprisingly, Fracer F. C did not observe any association of emotional stress during pregnancy with cleft lip or palate.^[7]

The association between the increased maternal age was supported by Bille *et al.*,^[11] Canela *et al.*,^[12] and Lebby *et al.*^[13] A study by Luo *et al.* reported that maternal age was significantly associated with congenital heart diseases, polydactyly, and cleft lip and/or palate relevant pregnancy,^[14] while Shaw *et al.* mentioned women older than 39 years had twice the risk than mothers between 25 and 29 years.^[15] The studies which denied the role of increased maternal age as an etiological factor for cleft lip and/or palate are by Vieira *et al.*^[16] and Robert *et al.*^[17]

In this study, the mean stress scores in mothers of nonsyndromic cleft children were higher than those of mothers of noncleft children. The mean maternal stress score in the cleft group was 17.58 ± 9.19 , while the mean maternal stress score in the noncleft group was 15.52 ± 8.33 . A significantly different distribution of stress levels was observed in both groups. In the cleft group, 40% of the participants had low-stress scores, 38% had moderate-stress scores, and 22% had high-stress scores. In the noncleft group, 58% of participants had low-stress scores, 28% had moderate stress scores, and 14% had high-stress scores. As per our analysis, the association between the high maternal stress scores and the occurrence of nonsyndromic cleft lip and/or palate was not found to be significant, ($P = 0.3220$, Chi-square = 2.2313).

A significant association was noted between increased maternal age and increased stress levels in the cleft group ($P = 0.0001$, Chi-square = 54.8230) [Table 1 and Figure 4]. High-stress scores were found to be 0% in the age group of 20–24 years, 10% in

25–29 years age group, 50% in the 30–34 years age group, while 100% in the 35–39 years age group. Out of 50, a total of 11 participants had high-stress scores. In the noncleft group, the association between increased maternal age and increased stress levels was not significant ($P = 0.3001$, Chi-square 7.230). High-stress scores were found to be 0% in the age group of 20–24 years, 6.06% in the 25–29 years age group, 23.53% in the 30–34 years age group, while 28.57% in the 35–39 years age group. Out of 50 participants, only 7 had high-stress scores [Table 2 and Figure 5].

The strength of our study lies in the fact that it elaborates and enlightens a very important and significant factor in the etiology of the nonsyndromic cleft lip and/or palate. However, it is not without any limitations. The main limitation of our study is the quantitative levels of the stress were measured, which relies purely on individual response and is mainly determined by the coping skill of the participant. Another limitation of this study is retrospective design. The data about the stress perceived during a prior period, i.e., during pregnancy collected retrospectively, may involve some amount of recall bias, which is difficult to avoid in such studies. Studies with an increased number of participants are needed to further confirm our results.

CONCLUSION

As per our analysis, no significant association was found between the increased stress scores and the occurrence of nonsyndromic cleft lip and/or palate. However, mothers of cleft children whose age was 35 years and above at the time of conception were noted to have higher stress levels. Increased maternal age associated with higher stress levels, in turn, increases the risk of nonsyndromic cleft lip and/or palate in the fetus.

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Conflicts of interest

There are no conflicts of interest.

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