e-ISSN 2371-770X

Modern Medical Laboratory Journal

DOI:10.30699/mmlj17.4.2.40

Evaluation of the Correlation between Socioeconomic Factors and Pediatric Cleft Lip and Palate

Mona Habibi[1], Shaghayegh Vahdat[1,*]

1. Department of Health Services Administration, South Tehran Branch, Islamic Azad University, Tehran, Iran

KEYWORDS

Cleft Palate;

Cleft Lip;

Biological Hazards;

Economic Factors;

Social Factors;

Family Factors

Article Info

Received 2021/11/01;

Accepted 2021/12/15;

Published Online 2021

ABSTRACT

Introduction: Cleft lip and palate is one of the most common congenital anomalies that affect the jaw, as well as the most common defects related to the lips and palate.

Objective: This study investigated the economic, social, and family factors affecting cleft palate.

Materials and Methods: PubMed, Google Scholar, Science Direct, and "SID" databases were used to investigate the correlation between births of children with cleft lip and palate and economic and social factors of the family. Finally, the most relevant titles and abstracts of articles were chosen to write this article.

Findings and Conclusion: In the present study, 13 studies were reviewed, and various factors were evaluated. The results showed a correlation between consanguineous marriage, genetics, smoking, no consumption of folic acid, increasing maternal age, poverty, and low education.

Corresponding Information: *Shaghayegh Vahdat, Department of Health Services Administration, South Tehran Branch, Islamic Azad University, Tehran, Iran. Email: Sha_vahdat@yahoo.com*

Abbreviations

SID, Society for information display; IranMedex, Indexing articles published in Iran biomedical journals; EMBASE, Excerpta medica database; OR, Odds ratio; CI, Confidence interval; RR, Relative risk; OFC, Occipitofrontal circumference; CLP, Cleft lip.

Introduction

Congenital malformations are common health problems that have lifelong consequences. For example, about 3% of all children in the United States are born with a congenital disability (1). Cleft lip and/or cleft palate are among the most common congenital disabilities and include cleft lip with or without a cleft palate or just cleft palate (2). The incidence of cleft palate is between 1 in 500 - 1 in 2500 births and varies according to the ancestral origin and socioeconomic status (3). The incidence of orofacial clefts is approximately 1 in 700 live births, and that 3200 new cases per year are expected with the population growth worldwide (4). The cleft lip and palate incidence occur at approximately 1 in 600 to 800 live births (1.42 per 1000), and cleft palate occurs at around 1 in 2000 live births. Thus, the typical distribution of cleft types includes; only cleft lip 15%, cleft palate and lip - 45%, cleft palate 40% (5). Many factors influence this anomaly, including genetic and environmental factors (6). Cleft lip and palate are associated with problems with nutrition, growth, cognitive development, speech, and behavior and require several surgical, medical, nutritional, dental, and other health interventions (7). Cleft lip and palate may significantly increase the risk of infant mortality, mainly when associated with other congenital disabilities (8). Several studies have found the decreased quality of life and psychosocial function among patients, partly related to low satisfaction with facial appearance (9, 10). The effects of cleft lip and palate may extend into adulthood and reduce psychosocial, educational, and economic gains (11).

Cleft lip and palate are believed to have multiple causes, including genetic predisposition and environmental influences, such as medication (12), age (13), smoking (14), alcohol (15), deficiency of vitamins and folic acid (16), sex and race, caffeine, benzodiazepines, corticosteroids as well as other occupational encounters. Maxillary, internal nasal, and nasal protrusions through the complex process of epithelial bridging, programmed cell death, and sub-epithelial-mesenchymal infiltration lead to epithelial fusion defects and involve many possible genetic factors or intracellular signaling pathways (17). Various epidemiological studies show that if one parent has a cleft palate, statistically, the probability of having a child with cleft lip and palate is 3.2, and having a child with a single cleft palate is 6.8% (18). If there is a cleft palate in one of the parents or a sibling, the probability of the next child's birth with cleft lip or palate is 15.8% and with cleft palate is 9.14%. In cases where one of the parents has a cleft palate, the probability that their child will be born with a cleft palate is 4.4% and with a cleft palate is 5.2% (19).

This study analyzed the correlation between economic, social, and family factors in neonates with cleft lip and palate. Very few review articles have evaluated the correlation between the factors affecting cleft lip and cleft palate. Many children with cleft lip and palate will undoubtedly face many problems related to their defects in their future lives. In this study, the assessment of the impact of socioeconomic factors of the Family on the pediatric cleft lip and palate has been addressed.

Materials and methods

The present systematic review manuscript was designed and implemented in 2021. Systematic articles were searched through databases containing Persian articles, including SID, Magiran, and IranMedex databases from 2008 to 2021, and English articles including Cochrane, EMBASE, Medline, and Google scholar from 2008 to 2021. This study used cleft lip, cleft palate, socioeconomic factors, genetic and environmental factors, and family history. Equivalent to these keywords was also searched in Persian databases. More than 500 articles were collected at first, of which 250 articles were initially deleted after reviewing the title. In the next step, 150 duplicate titles were removed. Then, according to the criteria, 20 articles remained. Finally, 13 articles were included in the present study.

Protocol

Selection of articles based on the desired criteria:

1. Selection of Persian and English articles,

2. Articles in the field of cleft lip and palate,

3. Articles about economic factors,

4. Papers concerning the impact of social factors,

5. Articles related to family factors,

6. Society statistics in infants with cleft lip and palate abnormalities.

Table 1. Selected articles based on the desired criteria

Author	Year of publication	Location	Duration	Sample No.	Anomalies No.	per 1000
Nahas *et al* (20)	2021	Syria	2016-2019	266	133	42/1
Aquino *et al* (21)	2011	Brazil	2006-2009	246	15	6/1
Yoshida *et al* (22)	2021	Japan	2011-2014	102104	234	7/23
Alrasheedi *et al* (23)	2021	Saudi Arabia	2016-2020	62088	99	6/1
Altoé *et al* (24)	2020	Brazil	2012-2014	878	150	NA
Taghavi *et al* (25)	2012	Iran	2005-2010	600	300	NA
Abdollahifakhim *et al* (26)	2016	Azerbaijan	2000-2015	670	670	NA
Cheshmi *et al* (27)	2020	Iran	2014-2020	723	323	NA
Ali *et al* (28)	2019	Sudan	2015-2016	288	133	4/1
Francisco *et al* (29)	2021	Swiss	1995-2015	266	133	4/1
Karina *et al* (30)	2020	Indonesia	2014-2018	604	91	NA
Salihu *et al* (31)	2014	Kosovo	1996-2005	304629	244	8/0
Liu *et al* (32)	2016	China	2002-2014	1319	213	NA

NA, not applicable.

Findings

Salihu et al. assessed family history, smoking, drug use during pregnancy, and parental age by mouth-opening in children in the Kosovo population. This study, conducted from 1996 to 2005 with a statistical population of 304629, included 244 anomalies. They found that heredity increased the risk of cleft palate in infants with OR= 8.25 and confidence interval=95% and CI=0.75-4.08, smoking with OR=87/1, confidence interval= 95% CI =0.82-12.5, use of drugs during pregnancy with OR =25.2, confidence interval =95 % CI=1.42-2.49, Increase in maternal age with OR=1.83 , confidence interval= 95%, CI=1.42-2.49 and increase in father age with OR =1.3, 95% confidence interval, CI=1.2-1.4 increases. Therefore, it was concluded that heredity is the most important cause of cleavage in Kosovo infants. They found that drug use and smoking were less important during pregnancy (31).

Abdollahifakhim et al. evaluated their studies in 2000-2015 with a statistical population of 670 anomalies. In this study, the age factors of mothers were 15-35 years (84.4%), and fathers were 15-35 years (64.3%), respectively. This age group is the most common time of delivery in Iran, and most abnormalities are seen at this age and older. Having a family history of a sibling (1.6%) with cleft lip and palate as much as a parent's disease (12.7%) affects a child's phenotype.

The most common affecting causes were smoking (7%), followed by depression (4.2%), hypertension (3.6%), severe anemia (3.4%), and diabetes (3.1%). Fortunately, smoking is rare in Iranian women, and most mothers are exposed to secondhand smoke due to their father's abuse. Psychotic illness, especially depression in mothers, was one of the dominant diseases in this study. Drug history was positive in 156 patients (23.3%) and harmful in 456 patients (68.1%). Drug history was ignored in 58 patients. The most common drug history in mothers was antibiotics (24 cases) (3.6%). Amoxicillin was much more common. Acetaminophen (6 patients), insulin (5 cases), and anti-shedding (5 patients) were in the following stages. Other drugs that had a lower dose (1 or 2 cases) were abortion drugs, antiemetics, and exposure to toxins 5.5% and 92.5% had a negative effect. Thirteen patients (1.9%) were missing. In this study, most patients (92.5%) did not live in high-risk areas, but most child families were urban splits (67.9% in urban areas and 29.1% in rural areas). The incidence of smoking, addiction, and alcohol abuse were 10.3%, 0.9%, and 0.4%, respectively. One of the most challenging factors in multifactorial diseases like schizophrenia is the father's job.

In this research, the most jobs are farmers (11.5%), followed by: employees (10%), transportation (8.5%), construction workers (5.8%), and metalworkers (4.9%). Most mothers (89.3%) were housewives, and only 3.3% were employed (26).

Aquino et al. studies conducted in Brazil in 2006-2009 showed that the disease was more common in children whose parents had a first-degree correlation history. In addition, cleft lip and palate were more common in men than women. Among the risk factors, only smoking was observed (21).

Cheshmi et al. conducted a study in 2014-2020 with a statistical population of 723 people, of whom 323 had cleft lip and palate abnormalities. A total of 171 children (53%) in the case group and 204 (51%) children in the control group were girls. Based on the results, 42 (13%) mothers of children with cleft lip and palate and 28 (7%) control mothers reported a history of miscarriage or abortion. Also, 119 (36%) mothers of children with cleft lip and palate and 93 (23%) mothers who witnessed consanguineous marriages reported. Examining mothers' medical records showed that 36 (11%) mothers of children with OFC and 32 (8%) control mothers suffered from at least one systemic disorder. Drug treatment during pregnancy was reported by 122 (38%) case mothers and 124 (31%) control mothers. The results showed that out of 92 (29%) mothers of children with cleft lip and palate, 88 (22%) mothers in the control group experienced complications during pregnancy. According to the results, the correlation between the birth of a child with the cleft lip and palate group and the sex of the child (OR=1.081, CI=0.45-1.80) Drug use during pregnancy (OR=1.351, CI=0.99-1.85), and a history of a systemic disorder (OR=1.44, CI=0.87-2.38) was not significant (P>0.05) (27).

Yoshida et al. Conducted a study in 2011-2014 with a statistical population of 98,787 children, of which 69 (0.07%) with cleft lip alone, 113 (0.11%) with cleft lip and palate, and 52 (0.05). %) were diagnosed with cleft palate within one month after birth. Considering the total result of oral cleft, statistically significant estimates of relative risk ratios (RR) for multivitamin intake before pregnancy (RR=1.71, CI=1.06-2.7) and during the first trimester (RR=2 .37 CI=1.8-3) was diagnosed. The results showed that the association between multivitamin intake after the first trimester was insignificant (RR=1.34, CI=0.59-3.01). Also, intake of maternal micronutrients through food was not associated with oral clefts in children.

Taking multivitamin supplements shortly before fertilization or during the first trimester of pregnancy is associated with increased cleft lip and palate at birth. Pregnant women and those planning to become pregnant should be aware of the potential dangers of multivitamin supplements (22).

Altoé et al. conducted a study in 2012-2014 with a statistical population of 878 out of 150 people with cleft lip and palate. The results showed that passive smoking, obesity, exposure to ionizing radiation, and antibiotics were associated with cleft lip and palate. The use of folic acid and analgesics were identified as preventive factors. The father's low level of education was considered a risk factor, while race/black was a preventive factor. However, these variables were not relevant in multivariate analysis (24).

Taghavi et al., in a study from 2005 to 2010 with a statistical population of 600 people, 300 of whom had anomalies; showed that low maternal age OR=1.06; confidence interval 95%; CI=0.007-0.074, socioeconomic status OR=0.36; confidence interval 95٪; CI=0.15-0.87, systemic maternal disease OR=0.36; confidence interval 95٪; CI =0.15-0.87, and maternal smoking OR=0.61; confidence interval 0.95%; CI=0.43-0.87, increased the risk of anomalies. There was a significant difference in iron and folic acid intake during pregnancy compared to the case and control groups. In assessing the risk of oral cleft palate, non-folic acid supplementation, maternal age, systemic diseases, and smoking should be considered risk factors (25).

Nahas et al. conducted a study in 2012-2016 with a statistical population of 233 people, 133 of whom included anomalies. Cleft lip and palate were slightly higher among men (51.9%). Family marriages accounted for 36.1% of the cases. 21.8% of the sample had first-degree relatives, and 24.8% had second-degree relatives born with cleft lip and palate. There were only 7 cases (0.05%) of cleft palate syndrome. Use of anticonvulsant drugs OR=10.73; confidence interval 95%; p=0.049, use of retinoic acid p=0.049; CI=0.95; OR=4.75, no consumption of folic acid p=0.00, CI=0.95; OR=28.23, smoking P=0.046; CI=0.95; OR=2, there was no association with maternal alcohol consumption or maternal diabetes p=0.65 (20).

Ali and Hamid (2016-2017, n=244), of whom 144 had anomalies, presented the following results. Low level of education (p=0.001), no folic acid supplementation (p=0.003, Cl=0.6-1; PV=0.014; OR=0.2) family history of gap (p=0.014, Cl=4.68-7.26; PV=0.01; OR=6) and low socioeconomic status (PV=0.042) had a significant relationship with cleft lip and palate. According to the results of multivariate analysis, maternal education was the most important factor, followed by folic acid supplementation (28).

Karina et al., in a study in 2014-2018 with a statistical population of 604 people, 91 of whom had cleft lip and palate abnormalities, showed that the correlation between maternal age and types of cleft lip and palate is P=0.628. There is no significant relationship between maternal age and any type of cleft lip and palate, while there is a relationship between the father's age and types of cleft lip and palate P=0.950, which indicates a non-significant correlation between the father's age and any type of cleft lip and palate. The relationship between maternal age and cleft lip and palate based on the age of the father group shows that there are no significant results for each of the paternal age groups, with a value of p=0.743 for the age of the young father; p=0.072 for the ideal age of the father, and p=0.448 for paternal age. The next statics shows the correlation between the father's age and the types of cleft lip and palate based on the age of the mother group. For the age group of young and ideal mothers, their p-value did not show a significant correlation (value p=0.393 for young maternal age and value p=0.941 for ideal mother age). The age of the elderly mother group shows a significant result with a value of p=0.045. Cleft palate occurs in infants born to an elderly mother (over 35 years old) (30).

In 1995-2015, Francisco et al. conducted a study with a statistical population of 266 people, 133 of whom had cleft anomalies. According to statistically significant factors related to parents, the probability of having a child with cleft lip and palate decreases per year of increasing maternal age (odds ratio = 0.903), and the likelihood of having a child with cleft lip and palate increases per unit body mass index (kg / m2) (odds ratio = 1.14). In the child's birth date, for each unit of mass (kg) increase, the probability of cleft lip and palate in the child decreases (odds ratio = 0.435). In this study, only maternal body mass index and maternal age showed statistical differences in the risk of having a gap child.

In the initial pediatric data, the cleft lip and palate group had a higher chance of being underweight at birth, but no correlation was found between head length and circumference (29).

Alrasheedi et al., in a study in 2016-2020 with a statistical population of 62088 with 99 abnormalities, showed that of males with mild cleft lip and palate (56.6%), 20 (20.2%) were the first child of the family, and 14 (14.1%) were the last (≥ 6) child. A quarter of children (26; 26.3%) were born with low birth weight (<2.5 kg), and 7 (7.1%) with a birth weight over 4 kg. The three children were premature and were born in the seventh month. Most reported risk factors among children include father smoking (50.5%), maternal smoking during pregnancy (45.5%), no folic acid supplementation during pregnancy (36.4%), history of previous abortions (31.3%), multivitamin deficiency during pregnancy (26.3%), gestational diabetes (11.1%) and irregular follow-up of pregnancy (25.3%). Family history of congenital anomalies and epilepsy were the least reported factors (8.1% and 2%, respectively). Regarding parental factors, kinship among parents of 60 children (60.6%) was reported. Forty couples (40.4%) had a first-degree, and 20 couples (20.2%) had second-degree relatives (23).

Liu et al. (2014-202, n=1319), including 213 cases, showed that the probability of cleft lip and palate increased with exposure to heat from cooking (adjusted odds ratio 4.1.1 Cl=1.2-4.5, 95%, OR=2.4) smoking (Cl=1.3-2.5, 95%, OR=1.8) was related. Women who are exposed to cooking (Cl=0.6-1.4, 95%, OR=0.9) compared to women who are not exposed to smoke. Children of women who were exposed to smoke were characterized by 1, 2, 3>4 smoke exposure (CI=0.6-1.8, 95% OR=1.1), (OR=1.4, CI=0.8-2.4, 95%), (Cl=1-3.2, 95% OR=1.8), (Cl=1.6-7.4, OR=3.4%, 95%) were associated, which show a clear trend, respectively. Therefore, it is concluded that exposure to smoke from burning coal and cigarettes causes cleft lip and palate in children (32).

Discussion

Cleft lip and palate are the most common congenital malformation of the head and neck (33). The overall prevalence for live births with cleft lip and palate is 1.42 per 1000 live births (34). Although its rate varies among different ethnic groups, its highest rate has been reported in Asia (35) and its lowest rate in Africa (36). These people have speech, hearing, and nutrition problems and suffer from social and psychological issues with age (37).

Cleft lip and palate is a multifactorial disorder due to genetic factors, triggers of cleft lip and palate syndrome, nutrition, smoking, alcohol consumption, nationality, geographical location, drug use, pesticides, folic acid deficiency, and low birth weight (38, 39).

Consanguineous marriage

Consanguineous marriage is a marriage in which the couple has a family relationship and has a common grandparent. In different societies, including Iran, intermarriage, especially among third-degree relatives (such as cousins), is not only common but also desirable. A study in Iran showed that about 38% of marriages occur between relatives. Due to the genetic commonalities of relatives, their children are more likely to develop autosomal recessive diseases (40). A study of children born in Zahedan hospitals over an 11-year period showed that among infants whose parents had hospital records, among infants whose parents had a hospital record, infants born in consanguineous marriages were about 4.5 times more likely to develop cleft lip and palate than infants born out of wedlock. About 82% of babies born with cleft lip or palate are born in consanguineous marriages (21). Kinship is considered an essential factor in autosomal recessive diseases. It has also been associated with congenital anomalies such as hydrocephalus, polydactyly, and CLP. The risk of congenital diseases in people born to first-degree consanguineous parents is higher than in non-consanguineous marriages (41).

Genetics

Congenital malformations are among the critical factors associated with mortality (42), hospitalization, and community disability, and approximately 3% of live births suffer from such malformations. Genetic factors, consanguineous marriage, drugs, and drug abuse are the most critical risk factors for congenital anomalies. The higher the proportion of common genes, the greater the risk of developing the disease. The proportion of common genes in third-degree relatives is about one-eighth (43). Genetic etiology has been available for many years to show that evidence from twin studies and segregation analysis confirms the genetic role in CL/P etiology. The risk of cleft lip and palate is higher when there is a positive family history, and the probability of having an infected child increases by 3 to 5 percent (44).

Moreover, the possibility of complications in the next child in parents who have a child with cleft lip and palate is 40% more (44).

Smoking

Parental smoking has been considered an essential determinant of developmental disorders (45). The effects of father smoking have a more negligible effect on the gap (46). Studies have shown a weak but significant association between maternal smoking and cleft palate. The aim of this study was to evaluate the relationship between active maternal smoking during pregnancy and childbirth with cleft lip and palate (especially in the first trimester of pregnancy) (43). However, we did not really see the effect of maternal smoking on the risk of gaps because the frequency of maternal smoking was very low, and smoking is often not culturally accepted by women in Iran. Smoking mothers also reduce their smoking rate after becoming aware of pregnancy (44). On the other hand, new studies have shown that smoking is definitely associated with cleft palate and increases its risk from 4 per 10,000 live births to 96 to 128 per 10,000 live births. For the first time, it was observed that children born to mothers who smoked during pregnancy had a larger cleft lip and palate ratio than mothers who did not smoke during pregnancy (46). Raut et al. (2019) reported that among 11 modifiable risk factors, including maternal age, alcohol consumption, folic acid supplementation, obesity, maternal education, diabetes, and fever, maternal smoking has the highest impact on CL/P (47).

Smoke from cooking

Indoor air pollution of solid fuels (coal or biomass) is a significant health threat. More than 70% of Chinese households rely on solid fuel for cooking and home heating (32). Combining coal and biomass inside the house produces significant amounts of toxic pollutants, including particulate matter, which is three times higher in rural homes (46). The results showed that exposure to cooking smoke was associated with congenital anomalies (48). This is the first study to report an association between home cooking with an open flame and a non-syndromic cleft. The probability of having a child with cleft lip and palate is almost 50% higher in mothers who are exposed to indoor cook smoke (48).

Taking medicine and cleft lip and palate

Taking medication during pregnancy is known to potentially not increase the risk of cleft lip and palate in children.

However, the independent analysis of drugs used by mothers during pregnancy was beyond our capacity. Our research shows that the most common medications used by mothers of children with cleft lip and palate during pregnancy include anti-stress drugs, abortion drugs, antibiotics, and some painkillers such as nonsteroidal anti-inflammatory drugs. Moreover, various studies (31, 49, 50) on the increased risk of cleft lip and palate following drug treatment are contradictory. We believe that it is not statistically reliable to report an absolute opinion for all drug classes, and it is recommended that each drug category be evaluated separately. The results of studies assessing the effect of a particular drug on the increased risk of cleft lip and palate are likely to be more conclusive.

Alcohol consumption

Maternal alcohol consumption during pregnancy can adversely affect the fetus. In addition, it can lead to a wide range of physical, behavioral, and neurological disabilities. The pattern and severity of these effects depend on the dose, time, pattern, and duration of alcohol use. It should be noted that the degree of vulnerability of different cells to alcohol varies from cell to cell. Animal studies have shown that alcohol exposure disrupts the cranial nerve cells and embryonic stem cells throughout the developmental stages of the fetus. In this study, it has been shown that the effect of alcohol depends on the amount of alcohol consumption (51). Growth defects due to alcohol exposure, including brain abnormalities, dysfunction of the central nervous system, and deficiency of developing organs and procedures of the growing body, have been observed. Maternal alcohol consumption has been reported to be associated with an increased risk of cleft lip and palate. In addition, it has been shown that children of mothers who drink alcohol are more likely to have cleft lip and palate than women who did not drink alcohol during pregnancy (52).

Multivitamin and folic acid

There is a relationship between taking multivitamin supplements during pregnancy and increasing the incidence of cleft lip and palate. In particular, compared to not taking supplements, taking before pregnancy confirmation or taking during the first trimester of pregnancy doubled the relative risk of cleft lip and palate. This association was significant even after adjusting for maternal factors and taking certain medications during pregnancy, although consumption after 12 weeks could not detect any significant association with oral cleft palate (22). In addition, in another study, not taking a multivitamin was associated with an increase in cleft palate and cleft lip and palate (28). A previous maternal multivitamin meta-analysis reported adverse outcomes in a group of 13,680 women with 1,418 cleft lip and palate children and the association between pre-pregnancy multivitamin intake and cleft lip and palate (53).

Social and economic factors

According to a study conducted by Kraples et al., low socioeconomic status and low education of the mother seem to be risk factors for having a child with oral clefts (54, 55). Low socioeconomic status should be considered a risk factor because it can indicate parents' health and lifestyle. People with low education smoke more, have an unhealthy diet, and receive fewer nutrients. Lifestyle factors, combined with occupational activities and genetic background, play a role in cleft lip and palate (25).

Conclusion

In this study, 13 manuscripts were reviewed, and various factors were evaluated. The results showed a correlation between consanguineous marriage, genetics, smoking, no consumption of folic acid, increasing maternal age, poverty, and low education. Indeed, the higher the proportion of common genes, the greater the risk of developing the disease. Genetic etiology showed that evidence from twin studies and segregation analysis confirms the genetic role in CL/P etiology.

Declarations

Funding
Not applicable.

Conflicts of interest

The authors declare no conflict of interest.

Authors' Contributions

M.H involved in methodology, and writing the original draft, S.V involved in conceptualization and methodology, and English polishing.

Ethical approval

Not applicable.

References

1. Control CfD, Prevention. Improved national prevalence estimates for 18 selected major birth defects--United States, 1999-2001. MMWR Morbidity and mortality weekly report. 2006;54(51):1301-5.

2. Wehby GL, Pedersen DA, Murray JC, Christensen K. The effects of oral clefts on hospital use throughout the lifespan. BMC health services research. 2012;12(1):1-17.

3. Mossey PA, Little J, Munger RG, Dixon MJ, Shaw WC. Cleft lip and palate. The Lancet. 2009;374(9703):1773-85.

4. Yılmaz HN, Özbilen EÖ, Üstün T. The prevalence of cleft lip and palate patients: a single-center experience for 17 years. Turkish Journal of Orthodontics. 2019;32(3):139.

5. Moyers RE. Handbook of orthodontics. 1988.

6. Wyszynski DF. Cleft lip and palate: from origin to treatment: Oxford university press; 2002.

7. Nackashi JA, Dedlow ER, Dixon-Wood V. Health care for children with cleft lip and palate: comprehensive services and infant feeding. Cleft lip and palate: from origin to treatment. 2002:127-58.

8. Wehby GL, Castilla EE, Goco N, Rittler M, Cosentino V, Javois L, et al. Description of the methodology used in an ongoing pediatric care interventional study of children born with cleft lip and palate in South America [NCT00097149]. BMC pediatrics. 2006;6(1):1-9.

9. Kapp-Simon K. Self-concept of primary-school-age children with cleft lip, cleft palate, or both. The Cleft palate journal. 1986;23(1):24-7.

10. Wehby G, Tyler MC, Lindgren S, Romitti P, Robbins J, Damiano P. Oral clefts and behavioral health of young children. Oral diseases. 2012;18(1):74-84.

11. Nopoulos P, Berg S, VanDemark D, Richman L, Canady J, Andreasen NC. Cognitive dysfunction in adult males with non-syndromic clefts of the lip and/or palate. Neuropsychologia. 2002;40(12):2178-84.

12. Park-Wyllie L, Mazzotta P, Pastuszak A, Moretti ME, Beique L, Hunnisett L, et al. Birth defects after maternal exposure to corticosteroids: prospective cohort study and meta-analysis of epidemiological studies. Teratology. 2000;62(6):385-92.

13. Materna-Kiryluk A, Więckowska B, Wiśniewska K, Borszewska-Kornacka M, Godula-Stuglik U, Limon J, et al. Maternal reproductive history and the risk of isolated congenital malformations. Paediatric and perinatal epidemiology. 2011;25(2):135-43.

14. Hackshaw A, Rodeck C, Boniface S. Maternal smoking in pregnancy and birth defects: a systematic review based on 173 687 malformed cases and 11.7 million controls. Human reproduction update. 2011;17(5):589-604.

15. Lorente C, Cordier S, Goujard J, Aymé S, Bianchi F, Calzolari E, et al. Tobacco and alcohol use during pregnancy and risk of oral clefts. Occupational Exposure and Congenital Malformation Working Group. American Journal of Public Health. 2000;90(3):415.

16. van Rooij IA, Ocké MC, Straatman H, Zielhuis GA, Merkus HM, Steegers-Theunissen RP. Periconceptional folate intake by supplement and food reduces the risk of nonsyndromic cleft lip with or without cleft palate. Preventive medicine. 2004;39(4):689-94.

17. Mehrotra D. Genomic expression in non syndromic cleft lip and palate patients: A review. Journal of oral biology and craniofacial research. 2015;5(2):86-91.

18. Banerjee M, Dhakar AS. Epidemiology-clinical profile of cleft lip and palate among children in India and its surgical consideration. CJS. 2013;2:45-51.

19. Vyas T, Gupta P, Kumar S, Gupta R, Gupta T, Singh HP. Cleft of lip and palate: A review. Journal of family medicine and primary care. 2020;9(6):2621.

20. Nahas LD, Alzamel O, Dali MY, Alsawah R, Hamsho A, Sulman R, et al. Distribution and risk factors of cleft lip and palate on patients from a sample of Damascus hospitals-A case-control study. Heliyon. 2021;7(9):e07957.

21. Aquino SNd, Paranaíba LMR, Martelli DRB, Swerts MSO, Barros LMd, Bonan PRF, et al. Study of patients with cleft lip and palate with consanguineous parents. Brazilian Journal of otorhinolaryngology. 2011;77(1):19-23.

22. Yoshida S, Takeuchi M, Kawakami C, Kawakami K, Ito S. Maternal multivitamin intake and orofacial clefts in offspring: Japan Environment and Children's Study (JECS) cohort study. BMJ open. 2020;10(3):e035817.

23. Alrasheedi AN, ALshaalan SF, Alruwaili HA, Zaid Alshalan SD, MT A. The Prevalence and Risk Factors of Cleft Lip and Palate in Northern Region of Saudi Arabia. Am J Otolaryngol Head Neck Surg. 2021;4(9):1158.

24. Altoé SR, Borges AH, Neves ATDSC, Aranha AMF, Borba AM, Espinosa MM. Influence of Parental Exposure to Risk Factors in the Occurrence of Oral Clefts. Journal of Dentistry. 2020;21(2):119.

25. Taghavi N, Mollaian M, Alizadeh P, Moshref M, Modabernia S, Akbarzadeh A. Orofacial clefts and risk factors in tehran, iran: a case control study. Iranian Red Crescent Medical Journal. 2012;14(1):25.

26. Abdollahifakhim S, Mousaviagdas M, Sohrabpour M. Study of risk factors related to the orofacial clefts in Eastern Azerbaijan, Iran: Population-based from 2000 to 2015. International Journal of Epidemiologic Research. 2016;3(4):336-44.

27. Cheshmi B, Jafari Z, Naseri MA, Davari HA. Assessment of the correlation between various risk factors and orofacial cleft disorder spectrum: a retrospective case-control study. Maxillofacial Plastic and Reconstructive Surgery. 2020;42(1):1-6.

28. Ali MAM, Hamid MMM. Risk factors of non-syndromic orofacial clefts in Sudan during 2016-2017. Annals of Medical and Health Sciences Research. 2019;9(1).

29. Francisco I, Caramelo F, Fernandes MH, Vale F. Parental Risk Factors and Child Birth Data in a Matched Year and Sex Group Cleft Population: A Case-Control Study. International Journal of Environmental Research and Public Health. 2021;18(9):4615.

30. Karina K, Fransisca F, Suryadinata KL. Analyzing Parental Age to Determine Types of Cleft in Hayandra Peduli Foundation Patient, Indonesia. Jurnal Profesi Medika: Jurnal Kedokteran dan Kesehatan. 2020;14(2).

31. Salihu S, Krasniqi B, Sejfija O, Heta N, Salihaj N, Geci A, et al. Analysis of potential oral cleft risk factors in the Kosovo population. International surgery. 2014;99(2):161-5.

32. Liu Y, Wang B, Li Z, Zhang L, Liu J, Ren A. Indoor air pollution and the risk of orofacial clefts in a rural population in Shanxi province, China. Birth Defects Research Part A: Clinical and Molecular Teratology. 2016;106(8):708-15.

33. Srivastava D, Ghassemi A, Ghassemi M, Showkatbakhsh R, Jamilian A. Use of anterior maxillary distraction osteogenesis in two cleft lip and palate patients. National journal of maxillofacial surgery. 2015;6(1):80.

34. Al Omari F, Al-Omari I. Cleft lip and palate in Jordan: birth prevalence rate. The Cleft palate-craniofacial journal. 2004;41(6):609-12.

35. Jamilian A, Jamilian M, Darnahal A, Hamedi R, Mollaei M, Toopchi S. Hypodontia and supernumerary and impacted teeth in children with various types of clefts. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;147(2):221-5.

36. Wehby G, Cassell CH. The impact of orofacial clefts on quality of life and healthcare use and costs. Oral diseases. 2010;16(1):3-10.

37. Golalipour MJ, Kaviany N, Qorbani M, Mobasheri E. Maternal risk factors for oral clefts: a case-control study. Iranian journal of otorhinolaryngology. 2012;24(69):187.

38. Cech I, Burau KD, Walston J. Spatial distribution of orofacial cleft defect births in Harris County, Texas, 1990 to 1994, and historical evidence for the presence of low-level radioactivity in tap water. Southern medical journal. 2007;100(6):560-70.

39. Saadat M, Ansari-Lari M, Farhud D. Short report consanguineous marriage in Iran. Annals of human biology. 2004;31(2):263-9.

40. Bakhshani S. Consanguineous Marriage and the Risk of Parents Having Children with Cleft Lip and Palate. International Journal of High Risk Behaviors and Addiction. 2021(In Press).

41. Carlson L, Hatcher KW, Vander Burg R. Elevated infant mortality rates among oral cleft and isolated oral cleft cases: a meta-analysis of studies from 1943 to 2010. The Cleft Palate-Craniofacial Journal. 2013;50(1):2-12.

42. Bittles AH. Endogamy, consanguinity and community genetics. Journal of genetics. 2002;81(3):91-8.

43. Khan AMI, Prashanth C, Srinath N. Genetic etiology of cleft lip and cleft palate. AIMS Molecular Science. 2020;7(4):328-48.

44. Xuan Z, Zhongpeng Y, Yanjun G, Jiaqi D, Yuchi Z, Bing S, et al. Maternal active smoking and risk of oral clefts: a meta-analysis. Oral surgery, oral medicine, oral pathology and oral radiology. 2016;122(6):680-90.

45. Raut JR, Simeone RM, Tinker SC, Canfield MA, Day RS, Agopian A. Proportion of orofacial clefts attributable to recognized risk factors. The Cleft Palate-Craniofacial Journal. 2019;56(2):151-8.

46. Ly S, Burg ML, Ihenacho U, Brindopke F, Auslander A, Magee KS, et al. Paternal risk factors for oral clefts in Northern Africans, Southeast Asians, and Central Americans. International journal of environmental research and public health. 2017;14(6):657.

47. Lacerda RHW, Furtado PGC, Vieira AR. Maternal Smoking Leads to Larger Cleft Palate Defects. Frontiers in Dental Medicine. 2021:26.

48. Auslander A, McKean-Cowdin R, Brindopke F, Sylvester B, DiBona M, Magee K, et al. The role of smoke from cooking indoors over an open flame and parental smoking on the risk of cleft lip and palate: A case-control study in 7 low-resource countries. Journal of global health. 2020;10(2).

49. Puhó EH, Szunyogh M, Métneki J, Czeizel AE. Drug treatment during pregnancy and isolated orofacial clefts in Hungary. The Cleft palate-craniofacial journal. 2007;44(2):194-202.

50. Zarante I, López MA, Caro A, García-Reyes JC, Ospina JC. Impact and risk factors of craniofacial malformations in a Colombian population. International journal of pediatric otorhinolaryngology. 2009;73(10):1434-7.

51. Bell JC, Raynes-Greenow C, Turner RM, Bower C, Nassar N, O'Leary CM. Maternal alcohol consumption during pregnancy and the risk of orofacial clefts in infants: a systematic review and meta-analysis. Paediatric and perinatal epidemiology. 2014;28(4):322-32.

52. de Andrade RS, Pedraza RM, Martellil DRB, Quiñones JAA, Júnior HM. Dental anomalies in fetal alcohol syndrome. A systematic. J Dent Res. 2020;4:1-5.

53. Wolf HT, Hegaard HK, Huusom LD, Pinborg AB. Multivitamin use and adverse birth outcomes in high-income countries: a systematic review and meta-analysis. American journal of obstetrics and gynecology. 2017;217(4): 404.e1-404.e30.

54. Krapels IP, Zielhuis GA, Vroom F, de Jong-van den Berg LT, Kuijpers-Jagtman AM, van der Molen ABM, et al. Periconceptional health and lifestyle factors of both parents affect the risk of live-born children with orofacial clefts. Birth Defects Research Part A: Clinical and Molecular Teratology. 2006;76(8):613-20.

55. Mirilas P, Mentessidou A, Kontis E, Asimakidou M, Moxham B, Petropoulos A, et al. Parental exposures and risk of nonsyndromic orofacial clefts in offspring: A case-control study in Greece. International journal of pediatric otorhinolaryngology. 2011;75(5):695-9.

How to cite this article: Habibi M, Vahdat S. Evaluation of the Correlation between Socioeconomic Factors and Pediatric Cleft Lip and Palate. Mod Med Lab J. 2021;4(2):40-49.