

Association Between Periconceptional Folic Acid Deficiency and Occurrence of Skeletal Anomalies in Newborns

Riasat Ali Nehra¹, Noor ul Mobeen¹, Akmal Bhatti² and Hafsa³

ABSTRACT

Objective: This study was planned to detect the connection among environs component (folic acid inadequacy) and development of Skeletal anomalies during intrauterine life.

Study Design: Case control study.

Place and Duration of Study: This study was conducted at the CLAP Hospital Johar Town and Arif Hospital Kasur from 1st January 2014 to 31st Dec. 2014.

Materials and Methods: It was a suitable sampling, two existing groups differing in outcome were identified and compared among, 100 sufferers of CLP and allied skeletal anomalies in neonates age not more than 6 months, in various Hospitals of Lahore. Mothers were asked whether they took folic acid or not during their early pregnancy.

Results: The skeletal anomalies number was quite high between mothers having deficiency of folic acid and other vitamins (11% as compared to 2.4% of controls).

Conclusion: Pregnant mothers who have not taken folic acid and other vitamins throughout their early pregnancy developed cleft lip with associated skeletal anomalies in their offspring.

Key Words: Skeletal anomalies, Environmental factors (folic acid and vitamins deficiency).

Citation of articles: Nehra RA, Noor ul Mobeen, Bhatti A, Hafsa. Association Between Periconceptional Folic Acid Deficiency and Occurrence of Skeletal Anomalies in Newborns. Med Forum 2018;29(1):56-59.

INTRODUCTION

There are many skeletal disorders more than 350.¹ Skeletal dysplasia is defined as generalized abnormality of the skeleton. Skeletal anomalies are usually associated with other facial (cleft lip) or organ system anomalies.⁴ These abnormalities are congenital or environmental teratogen exposure.⁵⁻⁸ Old persons had no knowledge regarding formation of baby during pregnancy.⁹

Teratogen effect skull and facial tissue development and with limb defects have also been caused by teratogens. A considerable number of cases of cleft lip and palate have associated skeletal anomalies. These anomalies in newborns varies as low as 4.3% to as high as 63.4% in which 13% are skeletal and 47% are cleft palate.¹⁰

Classification of Skeletal anomalies are commonly;

Syndactyly, It is fusion of one or more fingers and toes.

Polydactyly, This is presence of extra fingers or toes

Clubfoot, In this anomaly front part of the foot turns toward the inside of heel

Congenital hip dislocation¹¹. In this hip and thigh bones are underdeveloped and leads to dislocation of hip

Some rare limb anomalies are absence of finger, toes, or partial or complete absence of an arm or leg

Folic acid is a water soluble vitamin B and co-factor enzyme which is important for formation of purine and thymidine nucleotides and from homocysteine, methionine is synthesized. Deficiency of vitamin B result impaired folate and its deficiency leads to developmental anomalies like neural tube defects and associated skeletal anomalies. Disease can be limited by elevated folic acid intake in first trimester of pregnancy.¹²

The critical organogenesis period is, between six to nine week and deficiency of folate or low dose causes developmental anomalies¹³

One third of cleft lip cases with skeletal anomalies can be protected if folic acid is taken in first trimester of pregnancy, better nutrition and other vitamins intake have additional benefits.¹⁴ Multiple associated anomalies can occur due to environmental teratogens like folate deficiency. In a study at Jordan out of 44 associated anomalies 15.9% were skeletal anomalies¹⁵ In a study by Tolarova in 1982 high dose of folic acid (10mg) per day reduce the risk of congenital anomalies including skeletal anomalies¹⁶ Genes are also involved in congenital abnormalities but an interaction of genes

¹. Department of Anatomy Pak Red Crescent Medical and Dental College DinaNath, Kasur.

². Department of Community Medicine, Sialkot Medical College, Sialkot.

³. Department of Radiology, University of Lahore.

Correspondence: Riasat Ali Nehra, Assistant Professor, Department of Anatomy Pak Red Crescent Medical and Dental College DinaNath, Kasur.

Contact No: 0301-6880825

Email: drriiasat@yahoo.com

with nutritional deficiency enhances the pathogenesis of congenital anomalies¹⁷

Children with CLP and associated skeletal anomalies feel more anxiety. They respond differently as compared to normal children¹⁸

MATERIALS AND METHODS

Neonates having Cleft Lip or Cleft palate and allied skeletal anomalies who were brought by their mother for treatment in mentioned hospitals. Help was taken by concerned consultant. Neonate was entered according to inclusive criteria after taking permission from mother or close relative. This study was approved by Advanced board of King Edward Medical University Lahore.

Interview: A questioners, was framed and proforma was designed and different answers told by mother were entered on the questioners paper with special emphasis about intake of folic acid and supplementary vitamins.

Data analysis: Ninety-five percent confidence-interval, SPSS, 20.00 and Odds Ratio was estimated. Interval of introduction was outlined by Mean $\pm$ SD.

RESULTS

Folic acid and nutritional deficiency have been associated with cleft lip and palate and associated skeletal anomalies.



Figure No.1:Club foot

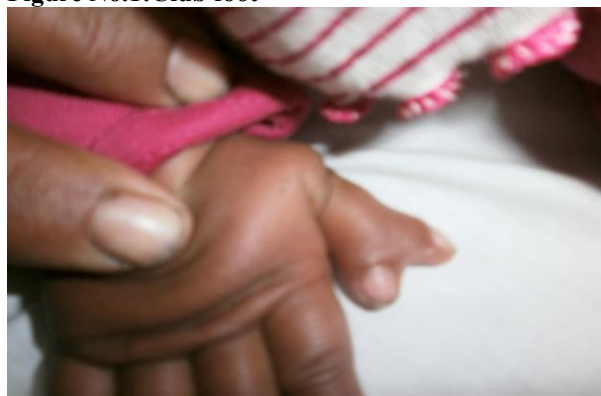


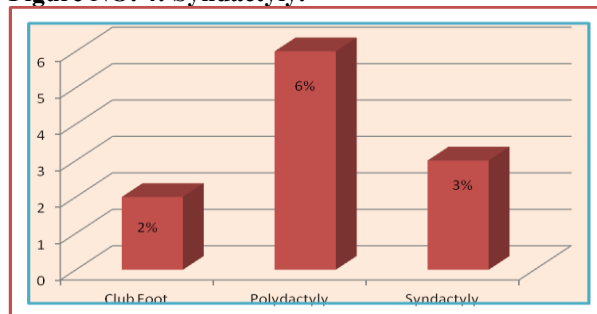
Figure No.2: Polydactyly



Figure No.3:Polydactyly with cleft lip



Figure NO. 4: Syndactyly.



Graph 1: Associated Skeletal Anomalies.

Table No. 1: Frequency of Associated Skeletal Anomalies Among Cases.

	Skeletal Anomalies	
	Yes	No
Club Foot	2%	98
Polydactyly	6%	94
Spina bifida	0	100
Club Hand	0	100
Syndactyly	3%	97
Total anomalies	11%	

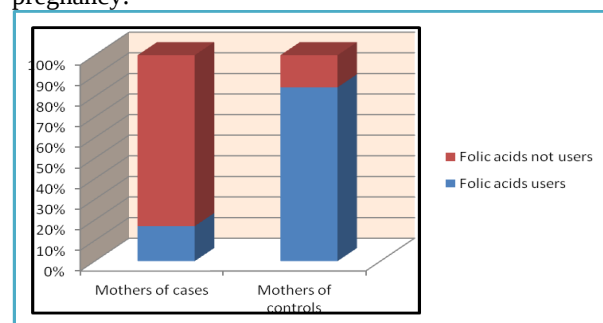
Table No. 2: Association Between of use of Folic Acid Tablets in Cases & Controls.

	Group	
	Cases	Controls
Yes	17	422
No	83	78
	100	500

Chi-Square Test= 24.34 p-value= 0.000
Odds Ratio= 26.41

Associated skeletal anomalies were seen in 11% of cases. The most common anomaly seen in 6% of cases was polydactyly, followed by syndactyly in 3% patients and 2% of patients had Club.

There were 17% patients whose mother told that during their pregnancy they used folic acid tablets, While 84.4% mothers of controls used folic acid tablets. Odds ratio was significant showing 26.41 times more risk if the mother does not use folic acid tablets during their pregnancy.



Graph 2: History of Folic Acid Intake

DISCUSSION

Results are variable between separate countries of studies. In connection to this research, so many components are responsible in the development of CLP with associated skeletal anomalies.¹⁹

In this study associated anomalies of the skeletal system with cleft lip and palate were studied which were present in 11% of the patients, polydactyly was the commonest 6% followed by syndactyly 3% and club foot 2% (table 1, Graph 1). The incidence of these anomalies may vary from as low as 4.3% to as high as 63%. Most common are the skeletal anomalies which account for 13% of the total.⁰ A retrospective study in Boy Town Hospital (USA) has reported orofacial anomalies followed by cardiovascular, central nervous system and skeletal anomalies.²⁰ In a study data from Sweden skeletal malformations were the commonest accounting for 33% of total malformation.²¹

The risk of orofacial with associated skeletal anomalies increases 26.41 times if the mother does not take any folic acid supplements during early pregnancy (Table 2, Graph 2). The protective effect of folic acid depends with dose and period of intake.¹⁴ A research conducted by Stoll and Wehby G, in Norway National and Iowa university respectively have reported a one third decrease in congenital anomalies including skeletal if 400 micrograms or more folic acid per day is taken by pregnant mothers.²² Our study is comparable with other studies as protective role of folic acid supplement against orofacial and skeletal anomalies.

CONCLUSION

At completion, the role of environmental component is revealed in this area for orofacial cleft development

with associated skeletal anomalies like club foot syndactyly and polydactyly etc. Taking into account of these outcomes, various issues can be addressed. Future planning for health of pregnant mother and baby can be made. Antenatal care is important for health of mother and taking additional nutrition and folates congenital anomalies can be avoided.

Author's Contribution:

Concept & Design of Study:	Riasat Ali Nehra
Drafting:	Noor ul Mobeen
Data Analysis:	Akmal Bhatti, Hafsa
Revisiting Critically:	Riasat Ali Nehra, Noor ul Mobeen
Final Approval of version:	Riasat Ali Nehra,

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

- Superti-Furga A, Bonafé L, Rimoin DL. Molecular-pathogenetic classification of genetic disorders of the skeleton. *Am J Med Genet* 2001; 106(2): 282–293.
- Hall CM. International nosology and classification of constitutional disorders of bone. *Am J Med Genet* 2002;113:65–77.
- Superti-Furga A, Unger S. Nosology and classification of genetic skeletal disorders: 2006 revision. *Am J Med Genet A*. 2007;143(1):1–18.
- Lachman RS, editor. Taybi and Lachman's radiology of syndromes, metabolic disorders and skeletal dysplasias. Philadelphia: Mosby Elsevier; 2007.
- Sutton VR, McAlister WH, Bertin TK, et al. Skeletal defects in paternal uniparental disomy for chromosome 14 are re-capitulated in the mouse model (paternal uniparental disomy 12) *Hum Genet* 2003; 113(1): 447–451.
- Walter CA, Shaffer LG, Kaye CI, et al. Short-limb dwarfism and hypertrophic cardiomyopathy in a patient with paternal isodisomy 14: 45, XY, idic(14)(p11). *Am J Med Genet* 1996;65(1): 259–265.
- Shanske AL, Bernstein L, Herzog R. Chondrodysplasia punctata and maternal autoimmune disease: a new case and review of the literature. *Pediatr* 2007;120:e436–e441.
- Savarirayan R. Common phenotype and etiology in warfarin embryopathy and X-linked chondrodysplasia punctata (CDPX). *Pediatr Radiol* 1999;29:322.
- Qritiz-Monastrop F, Serrano RA. Cultural aspects of cleft lip and palate treatment. In: Grabb WC, Rosenstein W, Bzoch KR, editors. *Cleft lip and palate*. Boston; 1971.p.319.
- Jenson BL, Kreiborg S, Dahl E, Fogh- Andersen P. *Cleft lip and palate in Denmark, 1976-1981*;

- Epidemiology, variability, and early somatic development. *Cleft Palate J* 1988; 25 (3): 285-69.
11. Campbell J, Henderson A, Campbell S. The fetal femur/foot length ratio: a new parameter to assess dysplastic limb reduction. *Obstet Gynecol* 1988;72: 181–184.
 12. Patrick J, Stover. Physiology of folate and vitamin B₁₂ in health and diseases. 2004;62(s1): S3-S12.
 13. Czeizel AE, Timar L, sarcozi A. Dose-dependent effect of folic acid on the prevention of orofacial clefts. *Pediatr* 1999; 104(6): 66.
 14. Bery RJ, Li Z, Erickson JD, Li S, Moore CA, Wang H, Wang H, et al. Prevention of neural tube defects with foic acid in china. *New Engl J Med* 1999;341 (20): 1485-90.
 15. Rawashdeh MA, Jawdat Abu-Hawas B. Congenital associated malformations in a sample of jordanian patients with cleft lip and palate. *Oral Maxillofac Surg J* 2008; 66(10): 2035-41.
 16. Talarova M. Periconceptional supplementation with vitamin and folic acid to prevent recurrence of cleft lip. *Lancet* 1982; 8291(2): 217.
 17. Richard HF, Gary MS, Edward JL, KERY LB, Suzan LC, Thomas HR. Gene- nutrient interactions: importance of folates and retinoids during early embryogenesis. Elsevier 2004;198(2): 75-85.
 18. Turner SR, Rumsey N, Sandy JR. Psychological aspects of cleft lip and palate. *Eur J Orthod* 1998; 20(4): 407-15.
 19. Saddler T W, Head and neck In: Langman s *Medical Embryology*.12th ed. Liponcott William and Wikins; 2011.p. 279-80.
 20. Beriaghi S, Myers SL, Jensen SA, Kaimal S, Chan CM,Schaefer GB, et al. Cleft lip and palate; Associated with other congenital malformation. *Ped Dent J* 2009; 33(3):207-10.
 21. Sekhon PS, Ethunandan M, Markus AF, Krishan G, Rao CB. Congenital anomalies associated with cleft lip and palate. *J Cleft Palate Craniofac* 2011; 48(4): 371-8.
 22. Wehby G. Folic acid and orofacial clefts: A review of the evidence. *Oral Dis* 2010; 16(1): 11-19.