NUTRITIONAL INTAKE PATTERNS OF PREGNANT WOMEN AS A CAUSAL FACTOR IN THE INCIDENCE OF CLEFT LIP AND PALATE: CROSS SECTIONAL STUDY AND BIBLIOMETRIC ANALYSIS

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Abstract

Problem statement: Nutritional intake patterns of pregnant women influence the occurrence of cleft lip and palate. Intake of macronutrients (carbohydrates, fats, proteins) and micronutrients (vitamin A, vitamin B12, folic acid) are at risk of causing cleft lip and palate (CLP). **Aim of the study**: to examine the relationship between the nutritional intake patterns of pregnant women and the incidence of CLP. **Methodology**: First, a retrospective cross-sectional study design was used with a sample of 49 respondents, mothers of patients with CLP who underwent labiopalatoplasty at Jember Lung Hospital from 2019 to 2024. The questionnaire included a Food Frequency Questionnaire (FFQ) and vitamin intake assessment. The FFQ was created by the National Cancer Institute. FFQ has indicators of carbohydrate consumption, fat consumption, protein consumption. FFQ is in the form of a likert scale. The vitamin intake assessment was adopted and modified from the supplement frequency questionnaire (SFQ) created by the American Society for Nutrition. Vitamin intake assessment has indicators: vitamin A consumption, folic acid consumption, and vitamin B12 consumption. Statistical analysis was conducted using the JMP statistical program with a significance level of $p < 0.05$. Second, a bibliometric performance analysis based on a literature meta-analysis of Scopus data from August 2024, which produced 1915 article metadata, was used. Network analysis, such as visualization of network metrics, clustering visualization, and density visualization, was conducted. **Main findings**: The study found that inadequate protein intake was associated with an increased risk of cleft lip and palate (odds ratio (OR) = 1.3346 times greater, 95% confidence interval (CI) = 0.0063–0.7530) than adequate protein intake, with a significant OR value (p-value 0.0283). In contrast, carbohydrate, fat, vitamin A, vitamin B12, and folic acid were not significantly associated (alpha >0.05) with p-values of 0.3524, 0.0523, 0.5674, 0.1622, and 0.5464, respectively. The mapping and clustering of research themes from 1915 articles revealed 7 clusters. However, only a few clusters had similar themes, namely, clusters 1, 2, and 4. **Conclusion**: There is a relationship between pregnant women's nutritional intake patterns and the incidence of CLP, especially regarding protein. Inadequate protein intake increases the risk of CLP than adequate protein intake. Research themes frequently discussed or studied between 2016 and 2018 dominantly addressed maternal nutritional status, non-syndromic cleft lip, nutritional problems, nutritional factors, nutritional deficiencies, adequate nutritional intake, unilateral cleft lip, bilateral cleft lip, CLP, and nutritional status.

Keywords: *CLP, Intake patterns, Nutrition, Risk factors*

1. Introduction

Non-syndromic cleft lip, with or without cleft palate, has severe long-term side effects on physical and psychological development. Despite significant improvements in clinical treatment in recent years, understanding the etiology of this congenital anomaly remains

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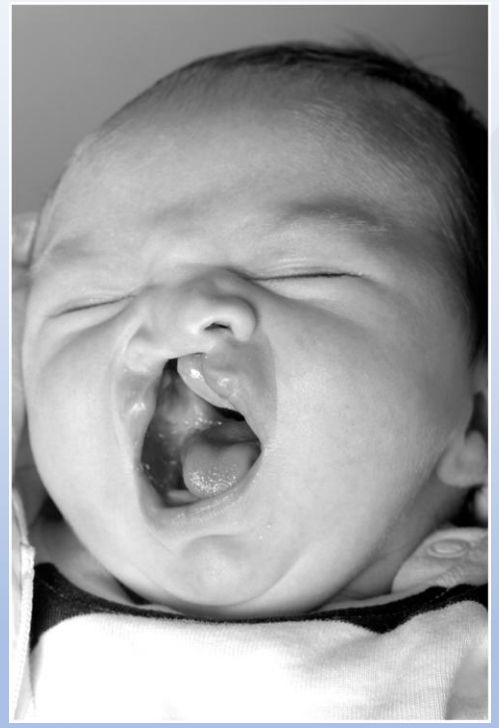
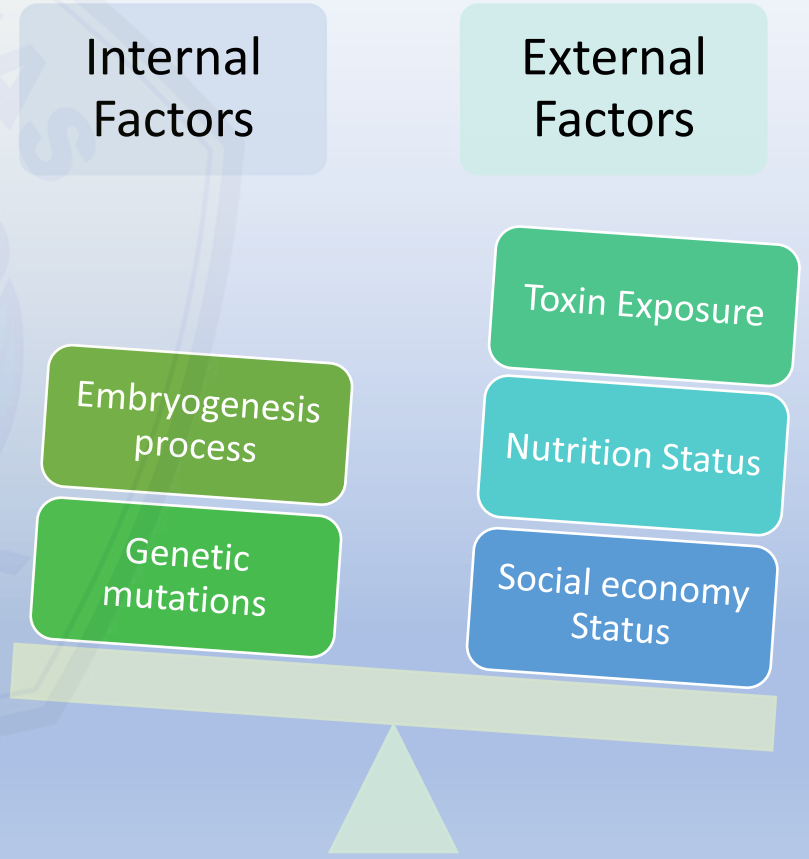
Introduction



Cleft Lip & Palate: the most often congenital anomalies in the world, affecting 1:1000 babies globally.

Gap in recent studies → vitamins consumed during pregnancy increase the risk of CLP (Mc Kinley, 2023)



Problem statement: Nutritional intake patterns of pregnant women influence the occurrence of cleft lip and palate. Intake of macronutrients (carbohydrates, fats, proteins) and micronutrients (vit A, B12, folic acid) are at risk of causing cleft lip and palate (CLP).

Aim of the study: to examine the relationship between the nutritional intake patterns of pregnant women and the incidence of CLP

Methods

Retrospective Cross-sectional study

- Samples are mothers of patients with CLP who underwent labiopalatoplasty at Jember Lung Hospital from 2019-2024
- 49 mothers with CLP babies

Tools

- Food Frequency Questionnaire (FFQ)
- Vitamin Intake Assessment Form (Vitamin A, Vitamin B12, Folic Acid)

Statistic Analysis

- Binary Logistic Fit (Logistic Regression) in JMP Statistic Tool
- Bibliometric Analysis

Patient Demography

Characteristic	Cleft lip n(%)	Cleft palate n(%)	Cleft lip and palate n(%)	Total n(%)
Gender:				
– Male	6 (13)	4 (8,6)	15 (32,6)	25 (54,3)
– Female	7 (15,2)	4 (8,6)	10 (21,7)	21 (45,6)
Education:				
– Primary–high school	10 (21,7)	5 (10,9)	19 (41,3)	34 (74)
– College–university	3 (6,5)	2 (4,3)	7 (15,2)	12 (26)
Occupation:				
– Unemployed	1 (2,1)	1 (2,1)	0 (0)	2 (4,3)
– Blue collar worker	7 (15,2)	4 (8,6)	14 (30,4)	25 (54,3)
– White collar worker	2 (4,3)	5 (10,9)	12 (26)	19 (41,3)
Income:				
– Under minimum wage	8 (17,4)	2 (4,3)	17 (40)	27 (58,7)
– Over minimum wage	5 (10,9)	5 (10,9)	9 (19,6)	19 (41,3)
BMI:				
– Underweight	1 (2,1)	0 (0)	0 (0)	1 (2,1)
– Normal	7 (15,2)	4 (8,6)	13 (28,3)	24 (52,2)
– Overweight	5 (10,9)	3 (6,5)	13 (28,3)	21 (45,6)

Characteristic	Cleft lip n(%)	Cleft palate n(%)	Cleft lip and palate n(%)	Total n(%)	p-value	OR (estimate)	95% CI
Carbohydrate							
– **Adequate consumption**	5 (10,9)	3 (6,5)	16 (34,8)	24 (52,2)	0,3557	0,4161	0,0744–2,5440
– **Inadequate consumption**	8 (17,4)	4 (8,6)	10 (21,7)	22 (47,8)			
Fat							
– **Adequate consumption**	9 (19,6)	3 (6,5)	18 (39,1)	30 (65,2)	0,0900	−1,2618	0,6744–230,688
– **Inadequate consumption**	4 (8,6)	4 (8,6)	8 (17,4)	16 (34,8)			
Protein							
– **Adequate consumption**	**5 (10,9)**	**3 (6,5)**	**20 (43,5)**	**28 (60,9)**	**0,0283**	**1,3346**	**0,0063 - 0,7530**
– **Inadequate consumption**	**8 (17,4)**	**4 (8,6)**	**6 (13)**	**18 (39,1)**			
Vitamin A							
– **Adequate consumption**	5 (10,9)	6 (13)	17 (40)	28 (60,9)	0,5689	0,2757	0,0864–3,8410
– **Inadequate consumption**	8 (17,4)	1 (2,1)	9 (19,6)	18 (39,1)			
Folic acid							
– **Adequate consumption**	11 (23,9)	7 (15,2)	23 (50)	41 (89,1)	0,5564	−0,4243	0,1381–39,5073
– **Inadequate consumption**	2 (4,3)	0 (0)	3 (6,5)	5 (10,9)			
Vitamin B12							
– **Adequate consumption**	10 (21,7)	7 (15,2)	18 (39,1)	35 (76,1)	0,1847	−0,7408	0,4928–39,2859
– **Inadequate consumption**	3 (6,5)	0 (0)	8 (17,4)	11 (23,9)			

Discussion

- Dietary intake is one of the **most common environmental factors** encountered and serves as a major driving force in evolution (Corella & Ordovas, 2009).
- Eating habits and nutritional intake are the most important environmental factors modulating gene expression throughout an individual's life (Yu et al., 2009; Kuzelicki et al., 2024).

CLP occurs due to disruption of palatal shelf growth, elevation, fusion, or epithelial breakdown during early embryogenesis (week 4-12 of gestation)

Caused by Nutrient Deficiencies → essential amino acid from animal source
- **Methionine**
- **Threonine**

Bezzera et al, 2015

Interrupted DNA synthesis, methylation, and regulation of craniofacial development genes

Bezzera et al, 2015

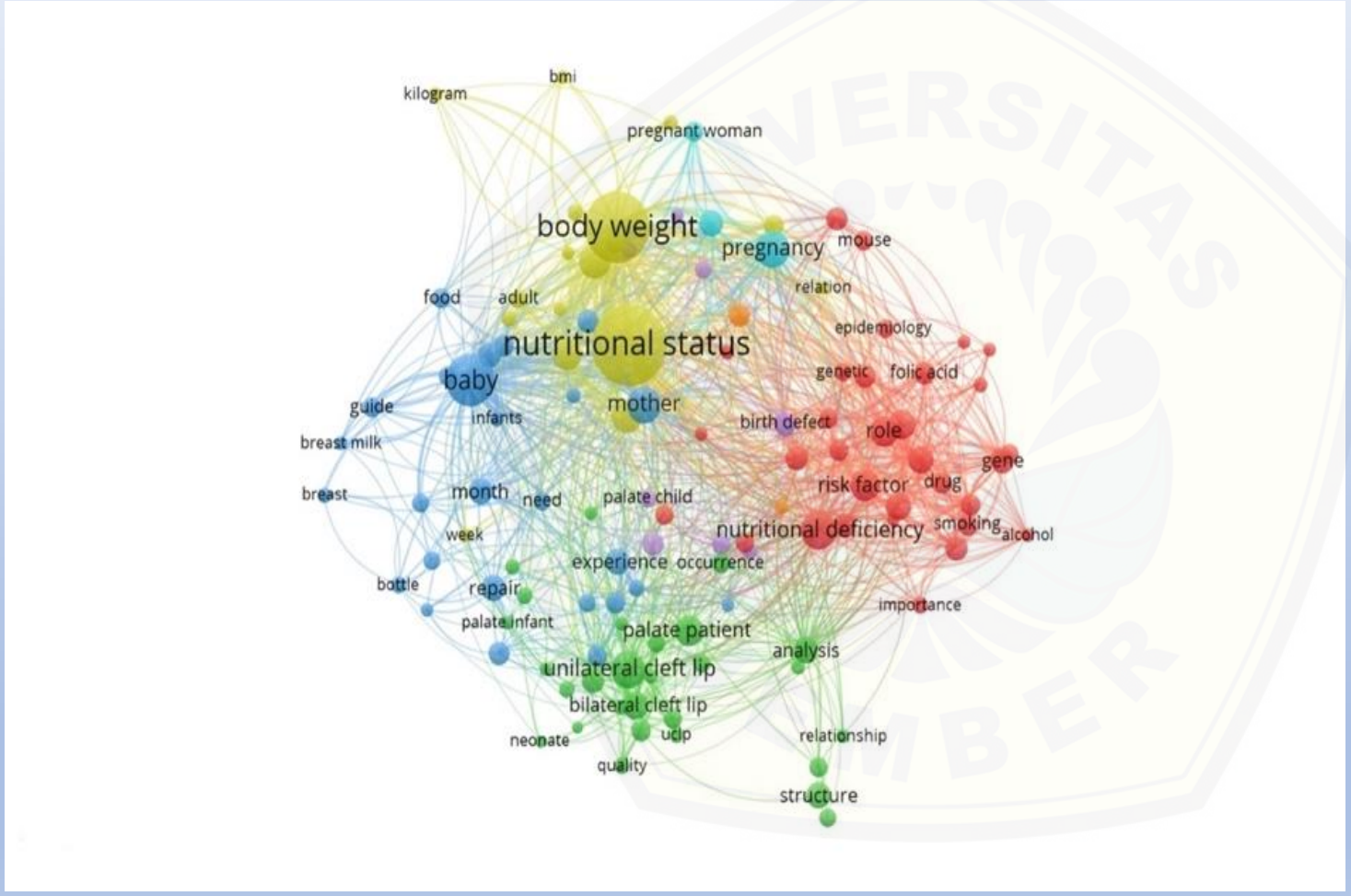
Not the single causes → multiple nutritional deficiencies (Folate, B12, Choline))

Salamanca et al, 2021

Discussion

- **Study by De-Regil et al (2015)** → Folic acid, alone or in combination with vitamins and minerals, prevents NTDs, but does not have a clear effect on other birth defects, such as CLP.
- This study shows that only protein consumption has significant association with the CLP incidence → **adequate supplementation** of micronutrient from Primary Health Care, but **inadequate macro nutrient (staple diet),** increase the risk of CLP due to methionine and threonine deficiency.
- Current Indonesian diet → high carbohydrate, high fat, high plant-based protein, **low animal-based protein**, low to medium vegetable and fruit consumption

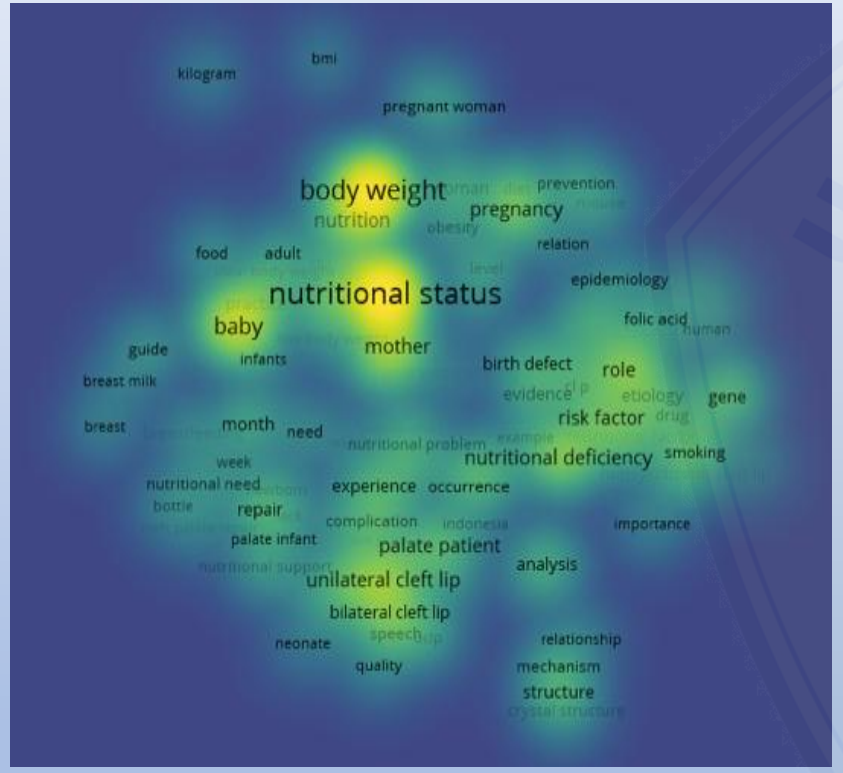
Bibliometric Analysis of the Cleft & Lip Palate Factors

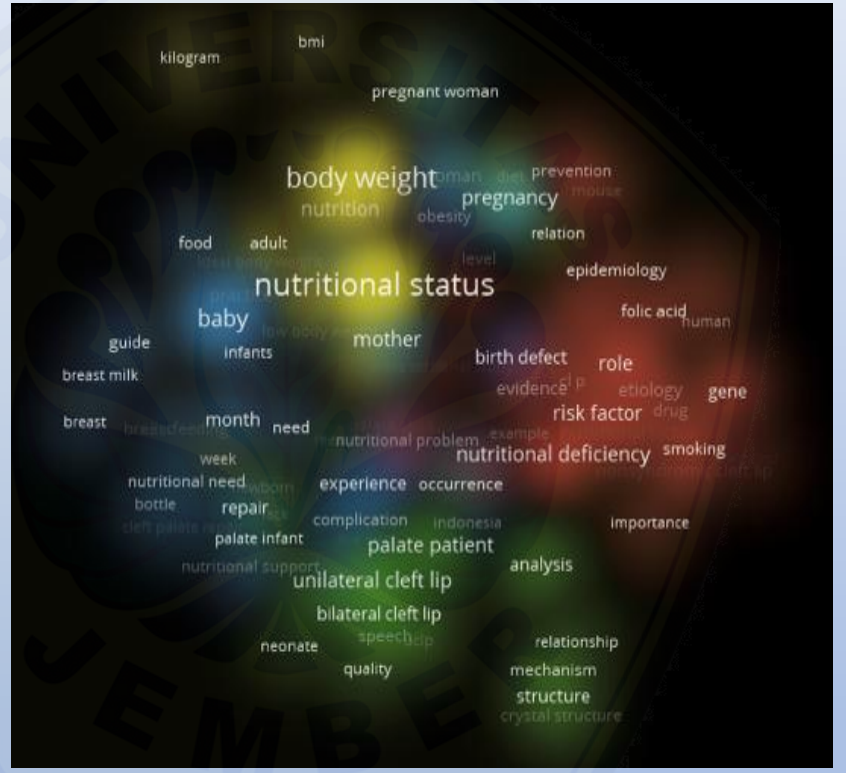


- **Maternal nutrition and deficiency** are central research topics in CLP.
- **Genetic–nutritional interactions** (red cluster) are widely studied.
- **Maternal anthropometry (BMI, body weight)** and **infant feeding/surgical repair** are important secondary themes.

- **Research gap:** Little direct focus on **amino acid deficiencies (methionine, threonine, protein)**

Density Visualization of the Research Intensity





- The density map highlights that **folic acid and general nutritional status** are the main focus in CLP research.

- **Amino acids (methionine, threonine, protein intake)** are missing from these hotspots → showing a **clear research gap**

Conclusion

- Protein deficiency has strong association with CLP incidence ($p<0.05$, OR 1.33, CI 0,0063 - 0,7530), likely due to deficiency of methionine and threonine, the limiting amino acids from animal-based protein
- Supplementation of vitamins and folic acid is important especially during 1st trimester, but the staple food consumption/macronutrient during pregnancy is equally important and need more attention
- This study has potential to fill the current research gap, however better study design needs to be done:
  - Reduce the bias with FFQ combined with meal pattern from the MCH book
  - More samples/respondents, in more hospital/health care
  - To minimize bias, FFQ or food recall should be done immediately after CLP diagnosis was made
  - Biochemistry analysis of methionine and threonine concentration from mother may give more accurate information of the deficiency status

THANK YOU FOR YOUR ATTENTION