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Incidence of Malnutrition between Preoperative Acyanotic and Cyanotic Congenital Heart Defect in Pediatric Patients: Systematic Review and Meta-Analysis

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ABSTRACT

Malnutrition has long known as an unfavorable outcome in congenital heart disease patients. Malnutrition may be differentiated into underweight, stunting, and wasting depending on anthropometric measurement. The difference of malnutrition prevalence and its subtypes in acyanotic and cyanotic congenital heart disease is currently unknown. This systematic review aims to elucidate the incidence of malnutrition, stunting, wasting, and underweight in cyanotic and acyanotic congenital heart disease (CHD) children. This systematic review is written in accordance with PRISMA guideline. Studies were searched on five different databases, and only cohort or case control studies are selected. The search was done using combinations of keywords and MeSH terms whenever eligible. Statistics was calculated by fixed-effect model with the Mantel-Haenszel method when there was no significant heterogeneity or with DerSimonian- Laird weights for the random-effects model when there was a significant heterogeneity. Two case control studies are included for review. No difference of general malnutrition and wasting prevalence between acyanotic and cyanotic CHD group. Stunting is substantially more prevalent in cyanotic CHD group (p=0,05). Underweight is more prevalent in acyanotic CHD, however the difference is not significant (p=0,11) Stunting represent a more severe impact in cyanotic CHD.

1. INTRODUCTION

Malnutrition in patients with congenital heart diseases (CHDs) has been linked to increased morbidity and mortality [1- 3]. In developing countries, cardiac-related malnutrition is a significant challenge affecting 50– 90% of children with symptomatic CHD [1]. The cause of malnutrition is multifactorial, includes genetic factors, inadequate caloric intake, and gastrointestinal tract immaturity [4]. Growth is a crucial

target in improving outcome in pediatric patients with CHDs [5]. However, studies investigating the malnutrition pattern in CHDs are still minimal. Thus, we aimed to compare the incidence of malnutrition between preoperative acyanotic and cyanotic congenital heart defect in pediatric patients using an evidence-based approach.

2. Methods

2.1 Eligibility Criteria

A meta-analysis was undertaken to compare the incidence of malnutrition between preoperative acyanotic and cyanotic congenital heart defect in pediatric patients. Studies that complied with following pre-specified criteria were included: (i) comparative studies of anthropometric profile in pediatric patients with preoperative acyanotic and cyanotic CHD; (ii) all cohort and case-control studies meeting the above criteria; (iv) performed anthropometric measurements according to standard World Health Organization (WHO) procedures; (v) reported the outcome of malnutrition based on WHO Z-score and (v) were published in the English language. The exclusion criteria were the following: (i) the subjects had undergone operative procedure prior to anthropometric measurements; (ii) cross-sectional and pilot studies;
(iii) studies conducted more than ten years ago; (iv) duplicate publication.

2.2 Search strategy

To identify all relevant literature meeting the pre-specified criteria, an electronic search for published articles (December 2020) was conducted in Google Scholar, ScienceDirect, PubMed, EMBASE, and Cochrane databases. Keywords and medical subject headings (MeSH) were used for specific searches. In each database, the MeSH terms “pediatric patients” or “children” were combined with the MeSH term “acyanotic congenital heart defect” and “cyanotic congenital heart defect. These terms were then combined with MeSH terms “malnutrition” or “failure to thrive”. The keyword terms corresponding to each of these MeSH terms were also mapped similarly. The search was further refined by searching for the following terms on the title or abstract fields of the retrieved citations: “pediatric patients”, “children”, “preoperative”, “congenital heart defect”, “anthropometric profile”, “nutritional status”, “malnutrition”, “failure to thrive”.

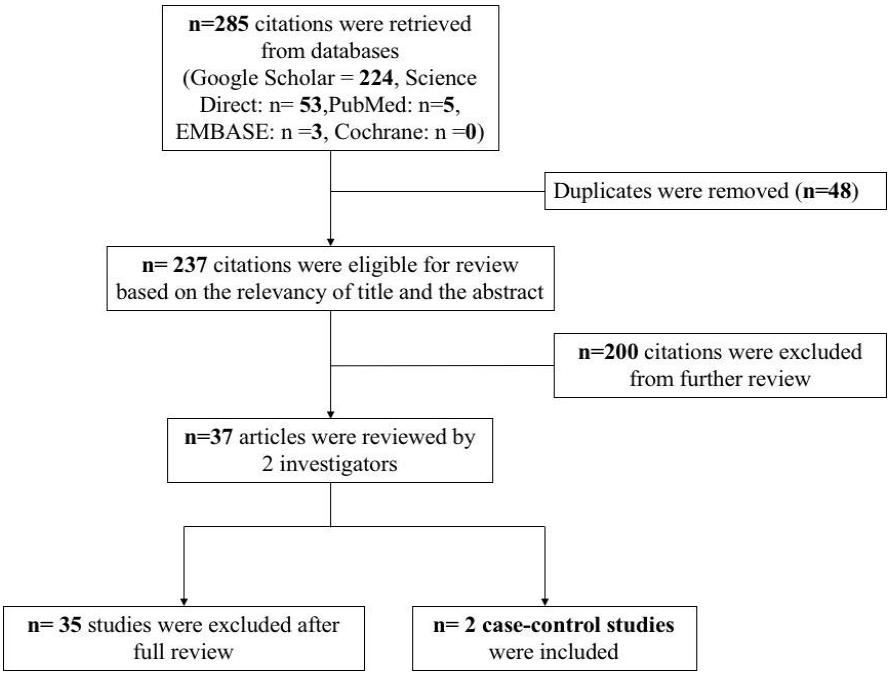

Figure 1 Search Strategy

2.3 Study selection

Two reviewers made the study selection. One for the citation screened and abstracts identified by the search strategies. Another one conducted full-text reviews to establish eligibility when screening reviewers believed that a citation potentially met the inclusion criteria. Disagreements of text inclusion were done by consensus.

2.4 Data extraction

Two reviewers independently extracted data from the eligible studies. The following information were extracted from each study: first author, year of publication, data source country, data collection period, study type, follow up duration, number of participants in each group (acyanotic or cyanotic), baseline characteristics and the outcome of malnutrition based on WHO Z-score, including: underweight (weight-for-age Z-score ≤ 2), wasting (weight-for-height Z-score ≤ 2), and stunting (height-for-age Z-score ≤ 2) (Table 1).

2.5 Statistical methods

Descriptive statistics method was used. The variables were presented as mean ± standard deviation and compared using the Student's t-test. The endpoints of each study were analyzed using risk ratio (RR) with 95% confidence interval (CI). The Cochrane Q test was used to assess the between-trial heterogeneity. The I2statistic was calculated as a measure of the proportion of the overall variation attributable to the between-trial heterogeneity rather than to chance, and we used the reported guidelines for low (I2= 25–49%), moderate (I2= 50–74%), and high (I2 ≥ _75%) heterogeneity. The overall effect size (RR) was calculated by fixed-effect model with the Mantel-Haenszel method when there was no significant heterogeneity (p > 0.10 or I2< 50%), or with DerSimonian-Laird weights for the random-effects model when there was a significant heterogeneity (p ≤ 0.10 or I2≥ 50%). Clinical outcomes were presented in forest plots. Publication bias with respect to the primary outcome (all-cause death) was assessed visually using a funnel plot. When there is no publication bias, studies of all sizes are scattered equally right and left of the line indicating the pooled estimate of natural log RR.

3. Results

3.1 Study Selection

From literature search, a total of two papers were deemed eligible and included in this review. Both of the studies are case-control study.6,7 The studies were done in Egypt, and Nigeria and all of them are published in English. A total of 173 patients were included in this review. Articles involved in this review included patients younger than eight years old as the subjects. For the case control studies, the patients were matched for the patients' age and sex, the two characteristics that could affect nutrition evaluation and nutritional status. The case control studies also had control group matched for the patients' age and sex. The studies were done on different times (2011 and 2015). Each of the studies was single centric.

The outcomes observed in each study were anthropometric parameters based on WHO growth chart, including weight-for-age Z (WAZ) score, height-for-age Z (HAZ) score, and weight-for-height (WHZ) Z score. A WAZ score of < -2 means that the patient is underweight, while HAZ score < -2 indicates stunting and WHZ score < -2 means wasting. Several demographics characteristics such as age, gender, gestational age, sex, birth weight, current weight, and current height were recorded to determine whether there was any different in baseline characteristics of intervention group compared to healthy control group. Data with normal distribution in each study was reported as means with standard deviations. Table 1 described the characteristics of the included studies.

Table 1 Baseline characteristics of the studies.

Study	Hassan (2015)	Okoromah (2011)	
Country (source of data)	Egypt	Nigeria	
Data collection period	2012-2013	2006-2008	
Study type	Case-control	Case-control	
Follow-up duration	N/A	N/A	
Number patients with acyanotic congenital heart defect	76/100	48/73	
Number of patients with cyanotic congenital heart defect	24/100	25/73	
Age range (months)	2-72	3-192	
Gender (males/females)	44/56	43/30	
Gestational age (weeks)		39.5 $\pm$ 0.85	39.4 $\pm$ 0.27
Birth weight (kg)	2.7	2.73.3	3.3
Underweight (WAZ $\leq$ 2)			
Acyanotic CHD	11	12	
Cyanotic CHD	1	2	
Wasting (WHZ $\leq$ 2)			
Acyanotic CHD	9	28	
Cyanotic CHD	11	2	
Stunting (HAZ $\leq$ 2)			
Acyanotic CHD	44	5	
Cyanotic CHD	8	17	
Exclusion of other cause of malnutrition	Performed	Performed	

The pooled analysis of general malnutrition status and each of malnutrition parameters can be seen at Figure 2-5. In general, malnutrition (Figure 2) and wasting status (Figure 5) does not differ between patients

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in acyanotic group than cyanotic group. However, the risk of stunting is significantly higher in cyanotic group compared to acyanotic group (p = 0,05), with both studies reported similar results. An exciting finding is observed when comparing the risk of underweight between acyanotic and cyanotic groups, in which both studies reported different outcomes. Meta-analysis of underweight status found that the risk of underweight is higher in acyanotic group, however the risk difference is not significant between the two groups (p = 0,11).

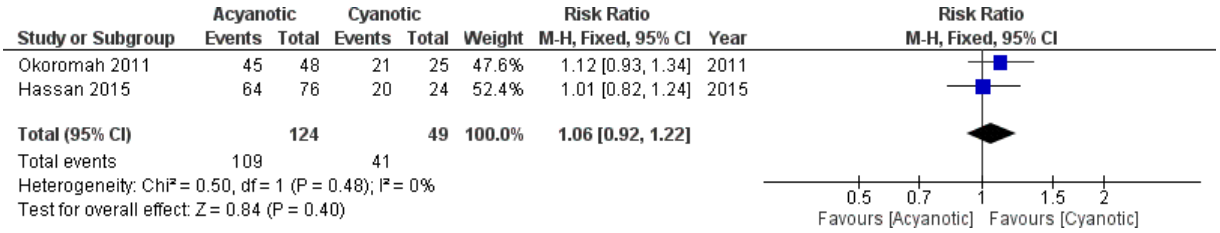

Figure 2 Forest plot of malnutrition status

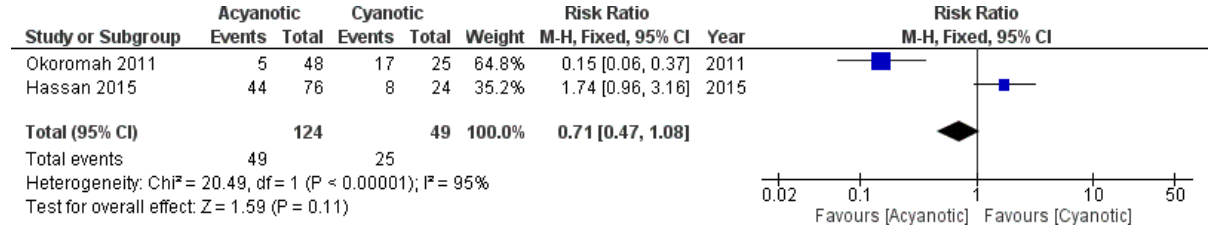

Figure 3 Forest plot of underweight status (WAZ < -2)

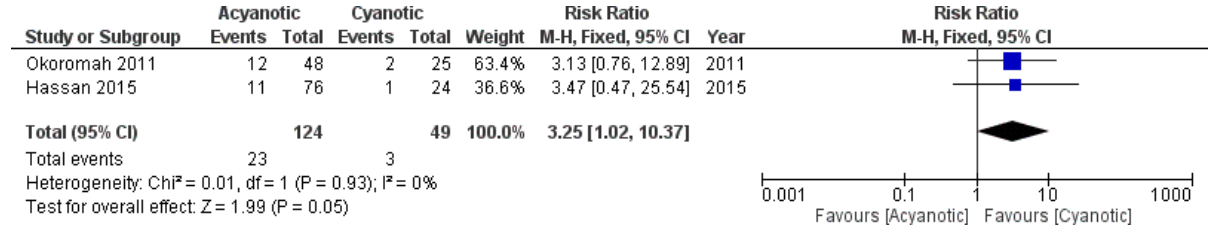

Figure 4 Forest plot of stunting status (HAZ < -2)

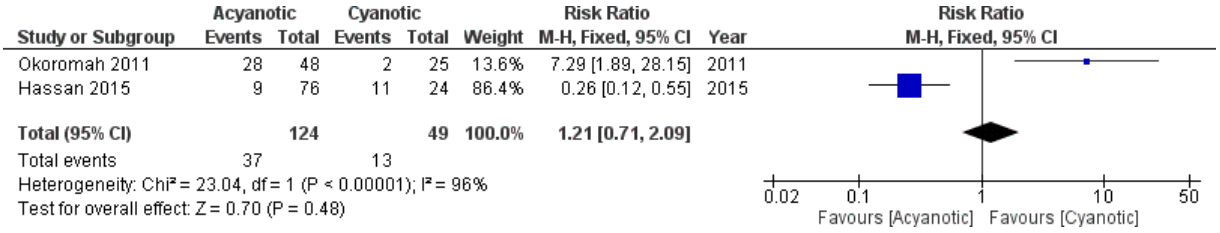

Figure 5 Forest plot of wasting status (WHZ < -2)

4. Discussion

This systematic review found that stunting is significantly higher in patients with cyanotic heart disease than acyanotic heart disease. [8] found that as high as 97% of children with cyanotic CHD have stunting, with severe stunting affecting up to 83% of the children. The results obtained from this review are consistent with other studies [9], [10]. However, another study found that the incidence of stunting is similar between cyanotic and acyanotic CHD [11]. Underweight is also prevalent in patients with CHD, and the incidence of underweight is higher than the average population. The same study by [8] found that underweight can be found in 100% congenital heart disease patients, with 76,67% afflicted by severe underweight. In this study, we found that the incidence of underweight is higher in acyanotic heart disease

group compared to cyanotic heart disease, albeit not significantly different. [12] reported similar results, with 31% of children with acyanotic heart disease were underweight compared to 23% of children with cyanotic heart disease. To this date, the exact pathophysiology of stunting and underweight in CHD has not been fully elucidated. However, past studies have found a correlation between impaired hemodynamic and decreased growth [13], [14]. Children with CHD, particularly the cyanotic, had less oxygen level in their bodies [15]. Direct and indirect effect of chronic hypoxia on insulin-like growth factor I (IGF-I) reduction leads to bone growth delay [16]. Decreased intake, increased energy requirements, malabsorption, poorly absorbed nutrition utilization, pulmonary hypertension, and the severity of heart disease influence the growth failure [17], [18]. Malnutrition is known to cause many different complications in children. It is usually described according to the anthropometric status comprising the weight and height of the child [19]. Wasting is defined as a low weight-to-height ratio. It is generally used as an indicator of acute nutrition deficiency. In contrast, stunting is defined as a low height-to-age ratio, which indicates chronic malnutrition characterized by hampered height growth velocity [20]. In developing countries, malnutrition was found to be associated with all-cause of child mortality, while in developed countries, it was correlated with duration of hospital stay and mechanical ventilation use [21].

CHD is the most prevalent anatomical anomaly in children. CHD was found to affect up to 8 out of 1000 children [22]. Children with CHD have an increased risk of malnutrition, both acute and chronic. The increased risk of malnutrition in children with CHD was caused by decreased nutrient intake and higher metabolic demands [23], [24]. High incidence of failure to thrive in children with CHD is caused by muscle wasting and reduction of subcutaneous fat due to caloric deficiency [25]. In developing countries, the incidence of malnutrition in children with CHD may reach 84%, with up to 71% of them afflicted with severe malnutrition [9] Malnutrition is especially striking in CHD patients with pulmonary hypertension, and nutritional status can be improved coherently with early treatment of the underlying congenital heart disease [26]. Furthermore, delaying postoperative feeding and nutritional treatment will further worsen the malnutrition of children with congenital heart disease [26], [27]. Congestive heart failure is the most popular complication that occurs in congenital heart disease patients. Interestingly, previous studies found that growth failure is the leading complication, followed by heart failure and pulmonary hypertension [28] Malnutrition was found to worsen the outcomes of pediatric congenital heart disease patients. Low weight-to-height is correlated with mortality and more prolonged mechanical ventilation in neonates with congenital heart disease [29]. Other studies also found that weight-for- age z-score is consistent with a higher incidence of infection, increased rate of mortality, and longer length of stay [30], [31]. Lower body fat percentage is related to a more extended period of mechanical ventilation and ICU stay in children undergoing surgical treatment for congenital heart disease [23]. Low calorie intake shows a relationship with a longer period of parenteral nutrition administration and undertaking open-heart surgery [32]. In addition, decreasing the weight-for-age ratio after surgical treatment mechanical ventilation after for CHD is associated with a higher mortality rate [33].

In the primary health care centers, awareness for congenital heart disease should be raised in children who presented with malnutrition. The physician's role in recommending the proper testing is essential for the child's development. Delayed recognition of congenital heart disease may result in fatal complications such as sepsis, shock, pneumonia, meningitis, and heart failure [28]. When detected at the earliest opportunity, intervention can be done immediately for catch-up growth and a better outcome [17]. To the author's knowledge, this is the first systematic review that assesses the difference of malnutrition parameters between acyanotic and cyanotic congenital heart disease. However, this study has some limitations. The amount of study included in this paper is very small, which will affect the generalization of this paper. The study included for review were case-control studies, which have lower levels of evidence than cohort

studies. We also did not account for the difference in diets between the cyanotic and acyanotic groups, which may act as confounding factors. Also, age group difference was not taken into statistical analysis. In the study by [6] the range of sample age varied between three months and eight years old. On the other hand, the range of sample age in the study by [7] was two months to three years old. In children, the age difference will affect lifestyle habits, dietary behavior, and the existence of long-term morbidity since children are actively growing along with age. Therefore, the difference in the age groups should have been factored into the statistical analysis.

5. Conclusion

Children with congenital heart disease, both cyanotic and acyanotic, have an increased risk of malnutrition. Specifically, children with cyanotic heart disease are more prone to stunting than children with acyanotic heart disease. Early detection and catch-up growth are essential for better outcomes. Further studies with larger samples are needed to determine the exact burden of malnutrition in each CHD.

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