Research Brief

Pre-pregnancy obesity and the risk of peripartum cardiomyopathy: A systematic review and meta-analysis

Iwan Cahyo Santosa Putra [a], Christian Bobby Irianto [a], Wilson Matthew Raffaello [b], Leonardo Paskah Suciadi [c], Hawani Sasmaya Prameswari [d, *]

[a] School of Medicine and Health Sciences Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia
[b] Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia
[c] Siloam Heart Institute/Siloam Hospital Kebon Jeruk, Jakarta, Indonesia
[d] Department of Cardiology and Vascular Medicine, Faculty of Medicine, Padjadjaran University, Bandung, Indonesia

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ABSTRACT

The outcome of this review is to assess the association between pre-pregnancy obesity and PPCM incidence. There were a total of 5.373.581 participants were included in this study. Pre-pregnancy obesity was significantly associated with PPCM incidence compared to normal-weight subjects (OR = 1.79 (1.16,2.76); $p = 0.008$; $I^2 = 59\%$, $P_{heterogeneity} = 0.04$). The sub-group analysis showed that pre-pregnancy women with obesity class I (OR = 1.58 (1.20,2.07); $p = 0.001$; $I^2 = 0\%$, $P_{heterogeneity} = 0.64$) and class II and III (OR = 2.65 (2.04,3.45); $p < 0.001$; $I^2 = 6\%$, $P_{heterogeneity} = 0.36$) was significantly associated with PPCM incidence compared to normal-weight subjects.

1. Introduction

Peripartum cardiomyopathy (PPCM) is an idiopathic cardiomyopathy with left ventricular (LV) systolic dysfunction, occurring in the last month of pregnancy until several months after parturition.[1] Among all of the risk factors associated with PPCM, obesity is one of the several modifiable risk factors of PPCM.[2] Recently, there are four observational studies showed that pre-pregnancy obesity was significantly associated with PPCM and another observational study found no significant association.[2–6] Due to equivocal results, this meta-analysis aims to evaluate the association between pre-pregnancy obesity with PPCM.

2. Methods

2.1. Search strategy

We performed a systematic literature search in adherence to PRISMA statement guidelines in several online databases using a broad search terms for "pre-pregnancy obesity" AND "peripartum cardiomyopathy". The search was started from inception until March 19, 2022. Any duplication were removed, and the remaining articles were manually screened for eligibility based on their titles and abstracts. All relevant articles were assessed by analyzing their full-text forms. Studies that did not fulfill our inclusion criteria were removed.

2.2. Selection criteria

Articles eligibility was assessed by two independent investigators and any discrepancies were resolved by discussion. We included observational studies containing pre-pregnancy obesity group, normal weight group and incidence of PPCM. Obesity was defined according to the World Health Organization criteria.[7] Whereas, PPCM diagnosis criteria was based on European Society of Cardiology guideline.[1] Any editorial, commentaries, reviews, and case reports/case series were excluded from this study.

2.3. Data extraction

Two authors carried out data extraction independently. We used a predesigned extraction form that comprised the authors, year of publications, country, category of BMI, PPCM criteria diagnosis, and study outcomes to collect relevant data from each included study. Quality assessment was carried out using the Newcastle–Ottawa Scale.

* Corresponding author.
E-mail addresses: iwantjoaa@gmail.com (I.C.S. Putra), christianbobbyirianto@gmail.com (C.B. Irianto), wilsonkores@gmail.com (W.M. Raffaello), be.bakerstreet@gmail.com (L.P. Suciadi), hawanisasmaya@gmail.com (H.S. Prameswari).

2.4. Statistical analysis

All statistical analyses in this study are using Review Manager 5.4.1 software. To describe the dichotomous variables, we used the Mantel-Haenzel formula to gauge the pooled estimates and its 95% confidence interval in the form of odds ratios. A two-tailed *p*-value ≤ 0.05 was considered statistically significant. Heterogeneity across studies was assessed by the inconsistency index (I^2) test, with a I^2 value above 50% or $p < 0,05$, demonstrating moderate to high heterogeneity.[8] We performed sensitivity analysis by leave one out method to conduct statistical robustness and assess the heterogeneity. If high heterogeneity was noted, a random effects model was assigned. The results of sub-group analysis, comprising obesity class I, II and III were assessed to gain a broad association between obesity and PPCM.

3. Results

3.1. Study selection and characteristic

The study flow is illustrated in [Fig. 1]. At the end of the study selection, we collected five observational studies[2–6] with a total of 5.373.581 participants. Total PPCM patients were 506 (0.001%) across of 5 studies. We merged the variable of obesity class II and III because differences in dichotomization of BMI were noted across the studies. The characteristics of included studies were describe in supplementary Table S4.

3.2. Meta-analysis of obesity and PPCM

This meta-analysis showed that pre-pregnancy obesity was significantly associated with PPCM compared to normal weight
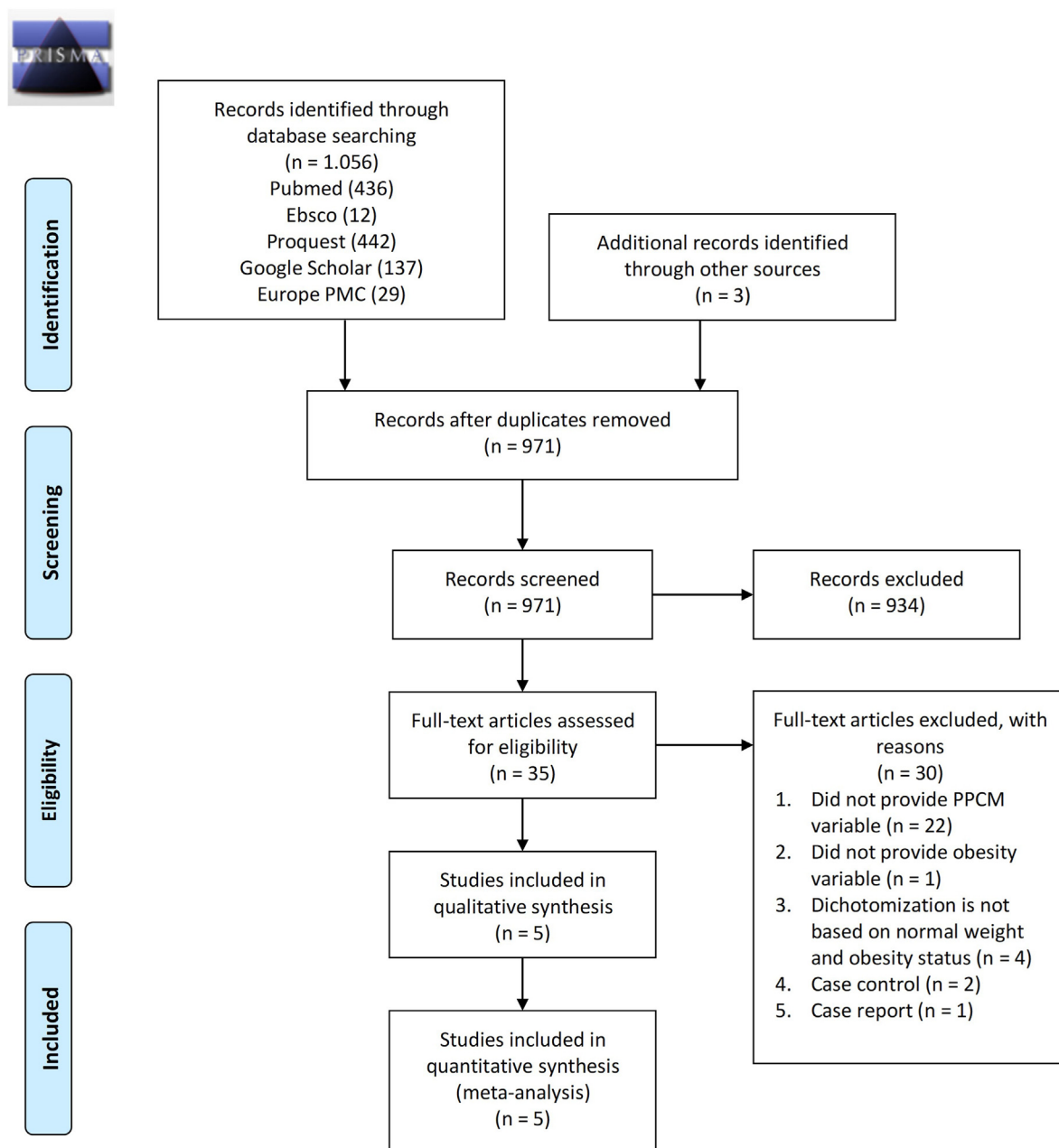

Fig. 1. Study flow diagram.

population (OR = 1.79 (1.16,2.76); p = 0.008; I^2 = 59%, $P_{\text{heterogeneity}}$ = 0.04) [Fig. 2]. Regarding moderate heterogeneity, we performed a sensitivity analysis by excluding the Nabbaale et al study resulting in a decrease of heterogeneity to 9% and increasing the odds ratio without altering its significance (OR = 2.04 (1.61,2.60); $p < 0.001$; I^2 = 9%, $P_{\text{heterogeneity}}$ = 0.35).

Sub-group analysis showed that pre-pregnancy women with obesity class I (OR = 1.58 (1.20,2.07); p = 0.001; I^2 = 0%, $P_{\text{heterogeneity}}$ = 0.64) and obesity class II and III (OR = 2.65 (2.04,3.45); $p < 0.001$; I^2 = 6%, $P_{\text{heterogeneity}}$ = 0.36) were significantly associated with PPCM [Fig. 2].

4. Discussion

This meta-analysis showed that pre-pregnancy obesity was significantly associated with PPCM. The significance was also obtained in sub-group analysis consisting population with obesity class I, II, and III. The odds ratio was highest in obesity class II and III group, followed by obesity class I, demonstrating a possible dose−response relationship.

In the sensitivity analysis, heterogeneity was significantly reduced after excluding Nabbaale et al study, as the only study consisting African predominance participants, showing that race might play a role related to obesity and PPCM incidence. Kao et al.'s study showed that pre-pregnancy obesity was associated with PPCM in the Caucasian race and Hispanic race but not in the African American race.[9] Consistently, an observational study from Nigeria also found that pre-pregnancy obesity was not significantly associated with PPCM and underweight subjects was more likely to get PPCM.[10] Hence, underweight group was probably more noxious compared to obesity group in term of increase risk of PPCM incidence in african race population.

There are three possible hypotheses of pathophysiology including hemodynamic changes, apoptosis, and inflammation. In obesity, high accumulation of fat alters circulating blood volume leading to an increased stroke volume which in turn causing LV wall stress, leading to eccentric LV hypertrophy, ultimately resulting in LV dysfunction.[11] Concurrently, pregnancy increases cardiac output through increasing stroke volume, which accounts for 45% and 55% in normal singleton and twin pregnancy, respectively.[12] Stroke volume will reach its peak at the end of the second trimester and may persist up to 12 weeks postpartum.[12] This phenomenon can cause reversible LV hypertrophy, leading to transient LV dysfunction during the third trimester.[13] Eventually, all of these hemodynamic changes contribute to PPCM.[13] Similarity was found between obesity and PPCM patients, whereby the level of inflammatory cytokines and biomarker of cell apoptosis in both conditions were significantly increased compared to healthy patients.[14,15] Thereby, a high level of proinflammatory cytokines and the apoptosis process in cardiomyocytes may result in LV dysfunction and remodeling, manifesting as heart failure.[13]
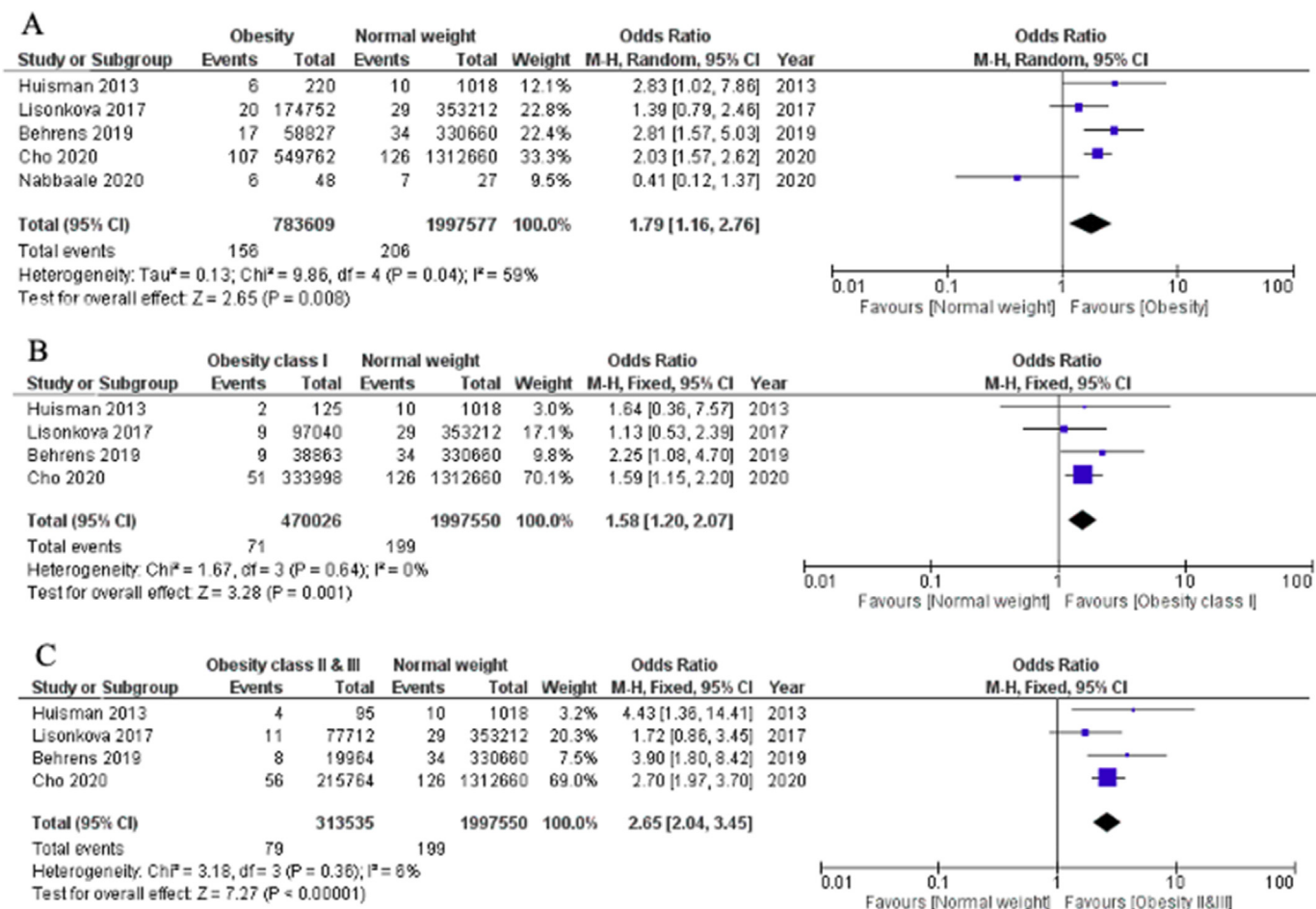

Fig. 2. Forest plot showing an association between obesity and PPCM. Legends (A) Obesity versus normal weight (B) Obesity class I versus normal weight (C) Obesity class II and III versus normal weight.

Despite promising results, there are several limitations in our study. Firstly, most of the studies were retrospective observational studies. Secondly, there is a moderate high heterogeneity due to race and ethnicity differences interstudy. Thirdly, BMI data from all included studies was collected from database or pre-tested study questionary which can increased the risk of bias. Fourthly, due to insufficient data in majority studies, only a few studies were included in this review.

In conclusion, this study suggested that patients with pre-pregnancy obesity is at higher risk of developing PPCM. To truly evaluate the impact of obesity on PPCM, prospective observational studies with heterogenous population are needed.

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Data availability

Available on reasonable request.

Ethical approval

Not Applicable.

Informed consent

Not Applicable.

CRediT author statement

Iwan Cahyo Santosa Putra: Conceptualization, Methodology, Formal Analysis, Data Curation, Investigation, Writing - Original Draft. **Christian Bobby Irianto**: Conceptualization, Methodology, Data Curation, Writing - Original Draft. **Wilson Matthew Raffaello**: Conceptualization, Methodology, Data Curation, Writing - Original Draft. **Leonardo Paskah Suciadi**: Data curation, Writing- Review & Editing. **Hawani Sasmaya Prameswari**: Investigation, Writing-Review & Editing.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2022.04.009.

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