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Association Between Postpartum Weight Retention and the Dietary Inflammatory Index

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by

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ABSTRACT

Objective: The objective of this thesis is to examine the relationship between the Dietary Inflammatory Index (DII), measured during the postpartum period, and postpartum weight retention.

Setting and Participants: We used the Infant Feeding Practices Study (IFPS) II (n=5000), a longitudinal study of women from late pregnancy through their infant's first year of life conducted between 2005 and 2007. Survey topics included feeding practices, infant health, food allergies, sleeping arrangements, mother's employment, childcare, and mother's dietary intake.

Main Outcomes: Postpartum weight retention **(**PPWR) was calculated in kilograms by subtracting self-reported body weight at 3, 6, 9, and 12 months postpartum from self-reported pre-pregnancy body weight. Substantial PPWR was defined as ≥ 4.55kg.

Methods: DII, a literature-based index, was used to measure the inflammatory potential of an individual's diet based on the Diet History Questionnaire (DHQ) collected by the IFSP II. A generalized estimating equations was used to examine the relationship between the DII score and PPWR and to determine the relationship between the DII score and the odds of substantial PPWR.

Results: For both outcomes of PPWR and substantial PPWR, the DII score was not a significant predictor (PPWR: 0.06 kg; 95% CI: [-0.11, 0.23]; P = 0.24) (Odds of substantial PPWR: 1.03; 95% CI: [0.96, 1.10]; P = 0.24). Time after delivery, marital status, parity, breastfeeding duration, pre-pregnancy BMI, and gestational weight gain were all significantly associated with PPWR and substantial PPWR.

Conclusions: This study did not find evidence that DII scores are associated with mean PPWR nor the odds of substantial PPWR. Time after delivery, marital status, parity, breastfeeding duration, pre-pregnancy BMI, and gestational weight gain were all significant covariates associated with PPWR and substantial PPWR. This study contributes to the literature on diet quality and PPWR and highlights the need for additional research examining if diet quality has a significant impact on PPWR.

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LIST OF ABBREVIATION

AHEI.. Alternative Healthy Eating Index
aMED.. Alternate Mediterranean Diet Index
ASA-24 .... Automated Self-Administered 24-hour Recall
BMI.. Body Mass Index
DHQ.. Diet History Questionnaire
DII® .... Dietary Inflammatory Index
DQIs.. Dietary Quality Indices
FDA... Food and Drug Administration
FFQ .... Food Frequency Questionnaire
FPL.. Federal Poverty Level
GDM .... Gestational Diabetes Mellitus
GEE... General Estimating Equations
GUSTO .... Growing Up in Singapore towards Healthy Outcomes
GWG .... Gestational Weight Gain
HEI .... Healthy Eating Index
HEI-SGP .... Healthy Eating Index Singapore
hsCRP .... highly sensitive C-Reactive Protein
IFPS II .... Infant Feeding Practices Study II
IL- .... Interleukin
IOM.. Institute of Medicine

MED.. Mediterranean Diet Score

MSD.. Mediterranean-style Diet

NCI.. National Cancer Institute

NHANES ....National Health and Nutrition Examination Survey

NICHD..................................National Institute of Child Health and Human Development

PPRW...Postpartum Weight Retention

SAA...Serum Amyloid A

SES...Socio-economic Status

TNF-α .... Tumor-Necrosis Factor-α

USDA...U.S. Department of Agriculture

WIC..Women, Infant, Child Program

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND

Obesity is a significant risk factor associated with adverse pregnancy outcomes[1]. Between 2011 and 2013, 16.9% of pregnancy-related deaths were among women who were obese before pregnancy[2]. About half of all women who become pregnant are overweight or obese[2]. This can lead to health complications for mother and child during pregnancy, labor, and child development. Women who are overweight or obese are at a higher risk for pregnancy-induced hypertensive disorders, preeclampsia, and gestational diabetes mellitus (GDM)[1]. During labor, obese and overweight women are more likely to experience a slower progression of labor, an increased risk for cesarean delivery, and more surgical complications[1]. These risks are not isolated to the mother; the newborns of obese and overweight women are also at an increased risk for being large-for-gestational-age, having shoulder dystocia, and experiencing premature delivery[1]. The impact of being overweight or obese during pregnancy does not stop after childbirth[1–4]. Women who experience GDM are at an increased risk for developing type 2 diabetes and preeclampsia which can put women at an increased risk for future hypertension and cardiovascular disease[2,3]. The developmental origins of health posits that most chronic diseases that occur in adulthood originate in vitro[4]. This can be seen in children of overweight and

obese mothers who are at a greater risk of being overweight or obese themselves and of developing other cardiometabolic health risks[1,4].

Overall women are at a greater risk for being obese compared to men and pregnancy and childbirth are windows of time for potential weight gain. The greatest weight gain for women occurs during their reproductive years, age 24-44 years old [1]. Weight gain during the reproductive years can occur before pregnancy (pre-pregnancy), during pregnancy (gestational weight gain, GWG), after pregnancy (postpartum), and in-between pregnancies (inter-pregnancy weight gain). During the postpartum period, weight gain is evaluated in terms of weight retained from pregnancy. Postpartum weight retention does not have a strict definition, but the general concept is described as excess weight retained from GWG[1].

Postpartum weight retention (PPWR) can contribute to women becoming obese after childbirth[1,5]. One important risk factor for PPWR is GWG[1,3,5–7]. Excessive GWG, beyond the Institute of Medicine's recommendations, can lead to greater PPWR, resulting in a higher pre-pregnancy body mass index (BMI) for subsequent pregnancies[3]. High pre-pregnancy BMI is also a risk factor for excessive GWG which then elevates one's risk for pregnancy complications such as GDM, hypertension, postpartum hemorrhage, and stillbirths [3]. There is mixed evidence that PPWR can be a significant risk factor for GDM in subsequent pregnancies[8,9]. Other risk factors for PPWR include being primiparous, having a under or normal pre-pregnancy BMI, having low early pregnancy vitamin D concentration (<64 nmol 1^{-1}), and breastfeeding for less than 6 months[6]. Endres and colleagues examined the risk factors associated with postpartum weight retention one year after delivery among predominantly low-income women[5]. Women in the Endres

study who retained at least 20 lbs were more likely to be African American, younger, poor, less educated, or on public insurance[5].

The American College of Obstetricians and Gynecologists in 2018 issued an opinion on Optimizing Postpartum Care recommending that women with chronic conditions such as obesity "be counseled regarding the importance of timely follow-up with their OBGYN or primary care provider for ongoing coordination of care"[10]. Understanding the relationship between diet quality and PPWR could influence care coordination and inform dietary recommendations to prevent and reduce PPWR. The relationship between diet and PPWR is not well studied.

There are clear recommendations on how women should adjust their diets during pregnancy[11,12]. It is recommended that during pregnancy, women increase their daily caloric intake by 300 kcal/day, allowing for possible adjustments due to age, pre-pregnancy BMI, and activity level[11,12]. Similar to pre-pregnancy dietary recommendations, carbohydrates should account for 45-64% and fats should account for 20-30% of daily macronutrients[11,12]. Protein intake should increase to 60g/day[11,12]. The Food and Nutrition Board of the Institute of Medicine (IOM) recommends an increase in intake of vitamin A, folate, vitamin C, iron, zinc, and more[11]. Yet there are little to no dietary recommendations for women that support postpartum weight lost[12,13]. Qualitative interviews conducted in Sweden among women about their knowledge and attitudes about PPWR found that women were not aware of the potential health risks associated with PPWR[14]. The interviews revealed excessive eating as a common strategy to combat emotional and physical discomfort and reported little to no postpartum weight loss support from the medical care providers[14]. Preliminary evidence among overweight and

obese women illustrates that dietary quality decreases during pregnancy and is maintained into the early postpartum period[15]. PPWR is a potential risk factor for adverse maternal outcomes, but the postpartum period is also a potential window of opportunity for intervention.

Historically diet has been evaluated by a single nutritional component such as iron or folate, yet this approach is inadequate due to collinearity, confounding, and effect modification since so many nutritional components are highly correlated[16,17]. Dietary Quality Indices (DQIs) address this problem by evaluating overall dietary patterns[16,17]. DQIs do this by using components of the index, partitioning each component, scoring and weighting, and then aggregating the scores of each component for a total score[16]. There are three types of DQIs: nutrient-based, food groups based on dietary guidelines, or a combination of the previous two[17]. Currently the most widely utilized DQIs is a combination of individual nutrition component intakes and food groups. The most popular DQI are the Healthy Eating Index (HEI), the Diet Quality Index, and the Mediterranean Diet Score (MDS)[17].

There is no consensus in the literature if a “healthier” DQI score leads to a lower PPWR[18,19]. This lack of consensus might be due to not accounting for inflammation. Obesity or excess weight can stimulate the release of inflammatory factors and inflammation contributes to the development of cardiovascular diseases[20]. Concentrations of individual inflammation markers differ over the course of pregnancy and into the postpartum period[21–24]. Pro-inflammatory markers, such as IL-6 and TNP-α show a slight increase of the course of pregnancy and then a slight downward trajectory starting either at birth or 6 months postpartum[21]. Several studies found the opposite trend for an anti-

inflammatory marker, IL-10, which followed a pattern of decreasing over pregnancy and then increasing after 6 months postpartum[21–23]. Evidence has also shown some inflammation biomarkers, C-Reactive Protein, concentrations to be linked to PPWR between 4-6 months postpartum[24]. Many studies found that pre-pregnancy BMI can have a strong influence in the trajectory of some inflammatory markers during pregnancy and into the postpartum period[21–24]. There is evidence that inflammatory markers are linked to PPWR[19,25] , but limited evidence that a 'healthy' diet, evaluated by DQIs, can reduce inflammation and promote postpartum weight loss [25–27].

There is no clear relationship between diet quality and PPWR that would allow for the development of dietary recommendations. There are indications within the literature that inflammation might play an intermediary role in the relationship between diet quality and PPWR[25,28,29], but the link with individual inflammatory markers do not provide a clear picture. The Dietary Inflammatory Index (DII®) evaluates and scores the inflammatory potential of an individual's diet based on any dietary reporting tool that can estimate micro and macronutrients. The DII® is a tool that can provide a more wholistic measure of dietary inflammatory potential.

1.2 PURPOSE AND SPECIFIC AIM

The purpose of this thesis is to examine the relationship between dietary inflammation, utilizing the DII®, and PPWR. The research question is to determine if there is a relationship between DII® score, measured during the postpartum period, and weight retained during postpartum. Based on limited previous findings, we hypothesize that a higher DII® score (i.e., more pro-inflammatory) is associated with increased mean PPWR and the odds of substantial PPWR.

CHAPTER 2

LITERATURE REVIEW

2.1 SEARCH METHODS

There have been no studies conducted examining the relationship between the DII and PPWR as of July 15, 2021, when this literature review was completed. Using the following terms: "postpartum weight retention", "dietary inflammation index", "maternal morbidity", "dietary quality index" (includes commonly used DQIs such as HEI and MED), and "inflammation", this review searched Academic Search, CINAHL, Health and Psychosocial Instruments, Health Source-Consumer Edition, Health Source-Nursing/Academic Edition, MEDLINE, APA PsychArticles, APA PsychInfo, Psychology and Behavioral Science Collection, and Pubmed databases. The results were limited to peer-reviewed articles in English published between 2009-2020.

2.2 FINDINGS

The literature review mostly resulted in studies that showed an association between a DQI and maternal and child health outcomes[30–49]. Some studies have found evidence that support DQIs being associated with maternal weight gain while others showed no associations[15,31,35,37,45,48,50,51]. DQIs come in various forms but the most widely used are the Healthy Eating Index (HEI), Diet Quality Index, and variations of the MDS[16,17,52]. Diet quality has also been linked to individual inflammation markers, which play a vital role on the disease pathway to GWG, PPWR, and other maternal morbidity conditions, such as preeclampsia[25,26,28,29]. There is some evidence that diet quality is

associated with maternal weight gain, especially during gestation and preliminary evidence linking dietary quality to individual inflammatory markers during pregnancy[25,26,28,29]. Yet, there is need for a study that examines the association between overall inflammatory potential of diet and PPWR.

Dietary Quality Indices

Before the development of dietary indices, in the field of epidemiology, a single nutritional component or food group was evaluated to better understand the nutritional risks of chronic diseases[16]. However, when these components are included in a statistical model examining the relationship between nutrition and chronic disease, many nutritional components and food groups are highly correlated resulting in multi-collinearity which can bias the findings[16]. DQIs aim to evaluate the overall diet and categorize an individual's diet as "healthy" or "not healthy"[17]. DQIs use dietary data such as food groups, like the amount of vegetables, or the amount of nutrients, like iron or fiber[16]. Following the selection of the index variables, decisions are made about where to partition the range of values for each variable[16]. This determines the cutoff point of when an individual has gotten a satisfactory or unsatisfactory amount[16]. Subsequently, each variable is scored, weighted, and aggregated to sum to an overall dietary quality score[16]. There are two approaches to defining dietary patterns used with DQIs: a posteriori approach or a priori approach[52]. A posteriori approach utilizes a statistical approach from dietary intake data gathered from the sample at hand to determine cutoff points for each index variable. In contrast, a priori approach operationalizes dietary variables used in an index beforehand based on current food guidelines[17,52].

DQIs can be divided into three types[17]. One major category is based on individual nutrients that are converted from food weights using food-nutrient tables[17]. The second category focuses on food group indicators and uses guidelines to dictate the appropriate portions and frequencies[17]. The last category of DQIs is a combination of the previous two and includes measures of diet variety, a measure of nutrients, foods to consume in moderation such as alcohol, and an overall balance of macronutrients[17]. HEI, Diet Quality Index, and the MDS, along with their individual variations, are all combination DQIs that take an priori approach [17].

The HEI was developed in 1995 and is based on ten components and has an overall score range from zero to hundred[17]. Five of the ten components are based on the five major food groups defined by the US Food Guide Pyramid and the following five components are based on aspects of the US Dietary Guidelines: limiting consumption of added sugars, sodium, saturated fat, and alcoholic beverages, and overall diet variety. Each of the ten components is scored from zero to ten[17]. In previous studies the HEI correlated positively with most nutrients in the body, BMI and with the study subject's self-perception of their diet[17]. The Alternate Healthy Eating Index (AHEI) attempted to improve upon this design by emphasizing the consumption of plant-based foods and unsaturated oils[17]. Studies have shown lower concentrations of inflammatory biomarkers and endothelial dysfunction to be correlated with higher AHEI scores[17].

The Diet Quality Index is similar to the HEI and AHEI but is based on dietary guidelines from the National Research Council of the USA and includes additional nutritional components, iron and calcium. The Diet Quality Index has two variety components that examine overall food group and within food group diversity. Eight

components consider adequacy of components that individuals should increase in their diet: vegetables, fruits, grains, fiber, protein, iron, calcium, and vitamin C; and five components that individuals should consume in moderation: total fat, saturated fat, cholesterol, sodium, and foods with low nutrient density (empty calories). The Diet Quality Index has had subsequent revisions since its inception in 1999 to reflect current dietary guidelines.

The MDS is made up of nine components: high monounsaturated to saturated fat ratio, moderate ethanol consumption, high consumption of legumes, cereals (including bread and potatoes), fish, and vegetables, and low consumption of meat and meat products, and milk and dairy products. The cut off for each component is determined by the sex-specific median and then assigned a value of 0 or 1 for unsatisfactory or satisfactory consumption, respectively. The total score then ranges from 0 (minimal adherence) to 9 (maximal adherence). The original MDS was developed and based on dietary consumption in Greece[53]. A later adaptation of the MDS, the Alternate Mediterranean Diet Index (aMED) was developed in 2005 and is used with a food-frequency questionnaire (FFQ). The aMED eliminates the dairy component, separates nuts and fruits into two components, and adjusts low moderate ethanol consumption to moderate alcohol intake. The aMED score, similar to AHEI, has also been associated with lower concentrations of inflammatory biomarkers and endothelial dysfunction[17].

This literature review only resulted in two articles that utilized the Dietary Inflammatory Index (DII®), this study's exposure of interest. The DII® is a DQI, based on micro- and macro nutrients and some individual whole food items and classifies an individual's diet as pro- or anti- inflammatory based on 45 food and nutrient

parameters[54]. An extensive literature review of 1,943 articles up to 2010 assessed the inflammatory potential of 45 food and nutrient parameters; from that literature review each parameter was scored [54]. Each parameter was given a score of '+1', if it caused a pro-inflammatory response, '-1', if it caused an anti-inflammatory response, or '0' if no change was observed [54]. After being weighted and adjusted based on the literature and world consumption means, an overall score was calculated[54]. An approximate overall score ranged from -9 to 8, with more negative scores representing an anti-inflammatory diet and more positive scores representing an pro-inflammatory diet [54].

Diet Quality in Pregnancy

Moran et al. used 301 overweight and obese women from the LIMIT randomized trial, to conduct a prospective cohort study[15]. Women in the study completed FFQ at 10-20, 28, and 36 weeks' gestation, as well as 4 months postpartum[15]. The data were then used to calculate HEI scores; 31% of the HEI scores at baseline were below average quality and these scores decreased across gestation and were maintained during the postpartum period (56.7 ± 12.7 vs. 53.3 ± 10.1, P<0.001)[15]. When analyzed by the individual nutrient components of the HEI score, the decrease was driven by decreases in milk, meat, and unsaturated oil and increases in the intake of solid fats, alcohol, and added sugars (P<0.001)[15]. In 2021, Hinkle et al. used data from the National Institute of Child Health and Human Development (NICHD) Fetal Growth Studies-Singleton Cohort. Within a sample of 1615 pregnant women from all pre-pregnancy BMI categories, Hinkle et al. showed that the majority of pregnant women did not meet the US Dietary Guidelines for nonpregnant females[37]. The study only found a decrease in HEI scores between the first and second trimester (65.9 [64.9,67.0] vs 51.6 [50.8,52.4])[37]. HEI scores

differed by race/ethnicity and pre-pregnancy BMI, with the lowest scores observed among non-Hispanic Black and obese women[37].

Dietary Quality, Gestational Weight Gain, and Postpartum Weight Retention

The primary objective for eight studies was to determine the association between dietary quality and gestational weight gain or postpartum weight retention[18,19,35,45,48,49,51,55]. Five studies examined GWG[35,45,48,49,51] and three studies examined PPWR[18,19,55].

Grandy et al. and Schlaff et al. both performed secondary data analyses on pilot prospective cohort studies with sample sizes of 41[35,48]. Both attempted to better understand the relationship between maternal diet quality during the second and third trimesters of pregnancy and GWG, but neither found any associations[35,48]. Grandy et al. analyzed data from a small study of pregnant women from Oregon Health & Science University Obstetric clinics from July 2012 to August 2013 between third trimester HEI score and GWG before (0.04kg [-0.18, 0.26]) and after adjusting for parity, maternal age, and pre-pregnancy BMI (-0.02kg [-0.24, 0.19])[35]. The Schlaff et al. study came to a similar conclusion and found that neither second trimester HEI scores (β=-0.13, P=0.53) nor third trimester HEI scores (β=0.03, P=0.84) were associated with GWG, though this study did not account for important covariates such as socioeconomic status (SES)[48]. The Schlaff et al. study did however, find a relationship between the greens and beans component of the HEI score and GWG during the third trimester (β=-1.67, P=0.04) that may indicate that increased intake of greens and beans might attenuate GWG[48]. Starling et al. chose to define diet quality by patterns of food group consumption within the

Healthy Start prospective cohort using reduced-rank regression[45]. This study found that a dietary pattern characterized by a high consumption of poultry, nuts, cheese, fruits, whole grains, added sugars, and solid fats correlated with GWG ($r=0.22$, $P<0.01$)[45].

Two studies did find evidence of a relationship between HEI scores and GWG, but were only able to observe this relationship if they modelled pre-pregnancy BMI as an effect modifier[49,51]. Parker preformed a secondary analysis of data from the Infant Feeding Practices Study II and found that both pre-pregnancy BMI and GWG were inversely associated with HEI scores ($P<0.01$)[51]. A significant interaction between pre-pregnancy BMI and GWG was detected ($P=0.04$) and in stratified adjusted models, the association between HEI scores and GWG differed depending on the individual's pre-pregnancy BMI category ($P<0.05$)[51]. The study hypothesized that higher HEI scores would be associated with adequate GWG, based on the Institute of Medicine's (IOM) recommendations, yet this was only seen in women with a normal pre-pregnancy BMI[51]. A study conducted within a cohort of Malaysian women, measured and calculated HEI scores in each trimester[49]. In this study, pre-pregnancy BMI was found to be an effect modifier, but the diet quality at each trimester also influenced their results. Yong et al. found that for non-overweight and non-obese women higher total HEI scores in the second trimester were significantly associated with a lower risk of inadequate GWG (aOR=0.97, 95% CI =0.95-0.99, $P=0.01$)[49]. While higher HEI scores in the third trimester were significantly associated with a higher risk of excessive GWG (aOR=1.04, 95% CI=1.01-1.07, $P=0.003$)[49]. Women with overweight/obese pre-pregnancy BMI, who had high HEI scores in either the second or third trimester had a significantly higher risk of

excessive GWG (aOR=1.04, 95% CI=1.01-1.07, P=0.02 and aOR=1.04, 95% CI=1.01-1.08, P=0.02)[49].

Three studies examined PPWR as the main outcome of interest. One study aimed to examine the association between prenatal diet quality and substantial PPWR in an Asian cohort[18]. The study evaluated diet quality using local prenatal dietary guidelines and quantified the HEI for pregnant women in Singapore (HEI-SGP)[18]. Diet quality of 687 women was measured between 26-28 weeks' gestation and substantial PPWR (≥ 5kg) was calculated at 18 months postpartum[18]. Lower diet quality, defined by a median score of 1.91 (95% CI: 1.17, 3.10) on HEI-SGP, was independently associated with the odds of substantial PPWR[18]. Stendell-Hollis et al. and Boghossian et al. both conducted studies examining the association between dietary patterns during the postpartum period and PPWR[19,55]. The Stendell-Hollis et al. study conducted a randomized controlled trial among 129 overweight women who were exclusively breastfeeding at a mean 17.5 weeks postpartum[19]. Women were randomized to adhere to a Mediterranean-style diet (aMED) or the U.S. Department of Agriculture's (USDA) MyPyramid diet for four months at 17.5 weeks postpartum[19]. Both groups of women demonstrated significant reductions in PPWR (-2.3 ± 3.4 kg for MED diet and -3.1 ± 3.4 kg for MyPyramid diet, both $P<0.001$) and no significant between-group differences were detected[19]. Boghossian et al. found no association between the alternative Mediterranean Diet Score (aMED) and the AHEI-2010 score and PPWR[55]. This study examined women who participated in the Infant Feeding Practices Study II [55]. No differences were observed in the mean PPWR over the follow-up period for either dietary pattern ($P>0.12$) [55].

Quality of Diet and Inflammation during Pregnancy

The literature review yielded four studies that provided preliminary evidence on the influence that diet can have on inflammation during pregnancy[25,26,28,29]. One study provided evidence to support the claim that metabolic changes that naturally occur during pregnancy elevate bodily inflammation[26], but diet can exacerbate or attenuate inflammation in the body [25,26,28,29]. Hrolfsdottr and Spadafranca were able to affirm a relationship between diet and individual biomarkers associated with inflammation[25,26]. Shin and Pieczynska employed the DII as their exposure variable and had mixed results in finding a relationship with DII and individual levels of biomarkers associated with inflammation among pregnant women[28,29]. All studies had cross sectional study designs, except Spadafranca and Pieczynska, who used a prospective cohort study taking measurements during the first and third trimester[25,26,28,29].

A cross sectional analysis of 671 pregnant women collected information about their diets using the FFQ and blood samples to measure the following biomarkers of inflammation: high-sensitivity C-reactive protein (hsCRP), serum amyloid A (SAA), interleukin (IL)-6, IL-8, IL-1β, and tumor necrosis factor-α at 30 weeks' gestation[25]. Driven by the consumption of animal protein, women in the highest protein intake quintile compared to the lowest had a 26% (95% CI: 3-54) higher concentrations of hsCRP and 23% higher SAA (95% CI: 4-47)[25]. Another study carried out among 99 normal weight White women from Milan, Italy, used the MDS as a measure of diet quality and discerned no changes in MDS scores from the first to the third trimester (P=0.7)[26]. This study examined adiponectin as a measure of inflammation[26]. Adiponectin is an adipose tissue-secreted cytokine, shown to improve insulin sensitivity, regulate metabolic glucose and lipids, and have a distinct antiatherosclerosis effects[26]. From the

first trimester to the third, concentrations of serum adiponectin decreased (-16% ± 4%, P=0.008), indicating increasing low-grade inflammation throughout pregnancy[26]. Though this study found support of diet attenuating this pattern, only women in the highest tertile of adherence to the MDS saw the lowest decrease in serum adiponectin (10% ± 11% vs. 34% ±3%, P=0.01)[26].

In a cross-sectional analysis of the National Health and Nutrition Examination Survey (NHANES) from 2003-2012, DII scores were estimated from a one-day 24-hour recall among pregnant women. Pre-pregnancy BMI, based on self-reported pre-pregnancy weight was found to be associated with lower DII® scores and higher concentrations of CRP[28]. After controlling for confounders like race, SES, and smoking status, women who were classified as obese, based on their pre-pregnancy weight, had increased odds for being in the highest tertile of DII® and CRP concentrations compared to women of normal pre-pregnancy BMI (aOR=2.40, 95% CI: 1.01-5.71 for DII and aOR=24.84, 95% CI: 6.19-99.67 for CRP)[28]. Among 45 pregnant, Polish women, inflammation biomarkers were shown to increase with DII® scores decreasing (meaning increasing overall dietary inflammation) from -1.78 in the first trimester to -2.71 in the third trimester, but this association was not significant (P=0.092)[29]. One randomized controlled dietary intervention trial that was conducted among 129 overweight women at a mean of 17.5 weeks postpartum showed that women randomized to 4 weeks of a Mediterranean-style diet had a significant reduction in the inflammation marker tumor-necrosis factor-α (TNF-α) between baseline and four months (change of -0.89 pg/mL, P=0.021) [19].

2.3 DISCUSSION

Several studies in this review provided evidence that diet quality among pregnant women does not meet nutritional guidelines[15,18,26,35,37,49,51]. Diet quality was also shown to be stagnant or decreased during gestation [15,26,35,48,49,51] and possibly remained low into the postpartum period[15].

Most studies examining GWG did not find an association between diet quality and GWG[35,48,49], but by analyzing single components of DQIs, there was evidence that individual and combinations of food groups can influence GWG[45,48]. Starling et al. found that dietary patterns could only explain five percent of the variation seen in GWG, after adjusting for confounders[45]. Two studies did find an association, but only when the analyses were stratified by pre-pregnancy BMI[49,51]. Pre-pregnancy BMI seems likely to be an effect modifier as this occurred in two very different populations using the same measure for dietary quality[49,51].

Inflammation appears to increase during pregnancy[21–24,26] and individual biomarkers appear to be associated with dietary components and overall DQI scores[25,26,28]. Previously mentioned studies in this review[49,51] identified pre-pregnancy BMI as a risk factor for GWG and the Shin et al. study found evidence that having an obese pre-pregnancy BMI increased the odds of inflammation and DII® scores during pregnancy[28]. Pieczynska and colleagues were not able to find similar results when looking at DII® scores during pregnancy and its correlation with inflammatory biomarkers[29].

The majority of studies examining the association between diet and GWG or PPWR did not measure diet quality from preconception to the first trimester[15,35,45,48,51]. These studies recommended that future studies consider the pre-pregnancy period as a time for potential intervention. Pre-pregnancy BMI was also seen as an important potential risk factor for GWG[49,51]. However; in 2011, 45% of all pregnancies were unintended[56]. The pre-pregnancy period would prove a difficult time to identify mothers who intend to have a child and have sufficient time to reduce their BMI from overweight/obese to normal.

There is mixed evidence that the DII® is a good measure for dietary inflammatory potential women during pregnancy and during the first year of postpartum[28,29]. But there is stronger evidence that diet plays an important role in regulating inflammation in the body[25,26,28]. DII® has been strongly linked to individual inflammation biomarkers[57,58], and could also be a good measure for potential dietary inflammation among pregnant and postpartum women. The DII® has yet to be used in a longitudinal study examining its association with PPWR among women who have recently given birth.

2.4 MOVING FORWARD

The aim of this current study is to examine the association between DII® and PPWR. PPWR is a risk factor for obesity that can affect the probability of entering into a subsequent pregnancy at a higher BMI, increasing the risk for pregnancy complications. Moran identified the postpartum period as a valuable time for intervention[15]. A meta-analysis of two randomized controlled trials showed that women who received a dietary intervention were more likely to have significant weight loss and to maintain this weight loss up to 12 months postpartum[59]. By understanding the relationship between diet,

inflammation, and weight retention, higher quality, evidence-based dietary recommendations can be developed for women in the postpartum period.

Table 2.1 Literature Review Results of Diet Quality, Inflammation, and Health Outcomes

Author, Time, Place	**Study Design, Sample Size**	**Study Objective**	**Diet Quality Measure**	**Outcome**	**Control Variables**	**Main Findings**
Moran et al., 2013, Australia	Prospective cohort study, n=301overweight or obese pregnant women	To assess the quality of diet in overweight and obese women during pregnancy and early postpartum	2005 HEI	Diet Quality measured by HEI	SEIFA, parity, age, ethnicity, smoking status, BMI, and gestational weight	31% of the HEI scores at baseline were below average quality and these scores decreased across gestation and were maintained during postpartum (56.7 ± 12.7 vs 53.3 ± 10.1, P<0.001)
Hinkle et al., 2021, U.S.	n=1817 pregnant women from NICHD prospective cohort	Characterize the diets of US pregnant women by trimester, race, and pre-pregnancy BMI	2010 HEI	Diet Quality measured by HEI	Age, race/ethnicity, native-born U.S., pre-pregnancy BMI, parity, marital status, education, prenatal/multivitamin at enrollment	The study only found a decrease in HEI scores between the first and second trimester (65.9 [64.9,67.0] vs 51.6 [50.8,52.4])[37]. HEI scores differed by race/ethnicity and pre-pregnancy BMI, with the lowest scores observed among non-Hispanic Black and obese women

Grandy et al., 2018, U.S.	Prospective, observational pilot study of 41 pregnant women in 3rd trimester	To understand the relationship between maternal diet, GWG, adiposity, and birth weight	HEI-2010	GWG	Pre-pregnancy BMI, maternal age, parity	No association between third trimester HEI score and GWG before (0.04kg [-0.18, 0.26]) and after adjusting for parity, maternal age, and pre-pregnancy BMI (-0.02kg [-0.24, 0.19])
Schlaff et al., 2020, U.S.	n=41 pregnant individuals participating in pilot behavioral intervention	Examine relationship between dietary quality in 2nd and 3rd trimesters and GWG	HEI-2015 from ASA-24	GWG	Age, race, gestational age, parity, education, marital status, and pre-pregnancy BMI	Neither second trimester HEI scores (β=-0.13, P=0.53) nor third trimester HEI scores (β=0.03, P=0.84) were associated with GWG
Starling et al., 2017, U.S.	n=1410 pregnant women from Healthy Start prospective cohort study	Identify dietary patterns associated with GWG and fasting glucose during pregnancy	Reduced-rank regression identified dietary patterns from ASA-24	GWG	Age, race/ethnicity, education, parity, smoking, physical activity, infant birth weight, infant sex, gestational age, and pre-pregnancy weight	A dietary pattern characterized by a high consumption of poultry, nuts, cheese, fruits, whole grains, added sugars, and solid fats correlated with GWG (r=0.22, P<0.01)
Parker et al., 2019, U.S.	n=1322 pregnant women from longitudinal IFPS II	To explore association between GWG, pre-pregnancy BMI, and diet quality	Alternative Healthy Eating Index for Pregnancy from Diet History Questionnaires	GWG	Age, energy intake, education, poverty income ratio, parity, race/ethnicity, WIC status, and smoking status	Both pre-pregnancy BMI and GWG were inversely associated with HEI scores (P<0.01). A significant interaction between pre-pregnancy BMI and GWG was detected (P=0.04) and in stratified adjusted models, the association between HEI scores and GWG differed depending on the individual's pre-pregnancy BMI category (p <0.05)

Yong et al., 2019, Malaysia	n=480 pregnant women from Seremban Cohort Study (SECOST)	To investigate association between diet quality in each trimester and GWG	HEI for Malaysians from one day, 24-hour dietary recall	GWG	Age, ethnicity, education, occupation status, monthly income, household size, parity, history of GDM, family history of diabetes, pre-pregnancy BMI, and physical activity	For non-overweight and non-obese women higher total HEI scores in the second trimester were significantly associated with a lower risk of inadequate GWG (aOR=0.97, 95% CI =0.95-0.99, p=0.01). While high HEI scores in the third trimester were significantly associated with a higher risk of excessive GWG (aOR=1.04, 95% CI=1.01-1.07, P=0.003). Women with overweight/obese pre-pregnancy BMI, who had high HEI scores in either the second or third trimester had a significantly higher risk of excessive GWG (aOR=1.04, 95% CI=1.01-1.07, P=0.02 and aOR=1.04, 95% CI=1.01-1.08, P=0.02).
Loy et al., 2019, Singapore	n=687 pregnant women from longitudinal Growing Up in Singapore towards Healthy Outcomes (GUSTO) study	To examine the association between circadian eating pattern and diet quality during pregnancy with substantial PPWR at 18 months	HEI-SGP from 24-hour diet recall	PPWR	Age, ethnicity, education, parity, employment status, physical activity, GWG, depression, sleep duration, bedtime, GDM, and mode of feeding	Lower diet quality, defined by a median score of 1.91 (95% CI: 1.17, 3.10) on HEI-SGP was independently associated with the odds of substantial PPWR

Stendell-Hollis et al., 2013, U.S.	Randomized, controlled dietary intervention trial of 129 overweight women, the majority of whom were exclusively breastfeeding	To compare postpartum weight reduction and inflammation among breastfeeding women who are randomized to either a Mediterranean-style diet (MED) of the USDA's MyPyramid diet for Pregnancy and Breastfeeding	Adherence to either a MED diet or MyPyramid diet	Postpartum weight reduction. Levels of inflammation marker tumor-necrosis factor-α	Age, ethnicity, education, infant age, formula supplementation, pre-pregnancy BMI, body fat, waist circumference, hip circumference, and waist/hip ratio	Both groups of women demonstrated significant reductions in PPWR (-2.3 ± 3.4 kg for MED diet and -3.1 ± 3.4 kg for MyPyramid diet, both P<0.001) and no significant between-group differences were detected. Women randomized to 4 weeks of a Mediterranean-style diet had a significant reduction in the inflammation marker tumor-necrosis factor-α between baseline and four months (-0.89, P=0.021)
Boghossian et al., 2013, U.S.	n=1136 women from longitudinal IFPS II	Examine PPWR and substantial PPWR with AMED and AHEI-2010 scores	Comparing AMED and AHEI-2010	PPWR and substantial PPWR	Age, education, race/ethnicity, marital status, poverty level, parity, smoking status, alcohol intake, breastfeeding, pre-pregnancy BMI, GWG, dietary characteristics	No differences were observed in the mean PPWR over the follow-up period for either dietary pattern (P>0.12)
Hrolfsdottir et al., 2016, Denmark	Cross-sectional analysis of 671 pregnant women	To examine association of diet and GWG with inflammation during pregnancy	Food Frequency Questionnaire	hsCRP, SAA, IL-6, IL-8, IL-1β, and TNF-α	Age, pre-pregnancy BMI, gestational age, GWG, birth weight, parity, smoking, education, total energy intake, protein, carbohydrates, and fats	Driven by the consumption of animal protein, women in the highest protein intake quintile compared to the lowest had a 26% (95% CI: 3-54) higher concentration of hsCRP and 23% higher SAA (95% CI: 4-47)

Spadafranca et al., 2018, Italy	Longitudinal cohort study of n=99 normal weight Caucasian	To examine if adherence to MedDiet in 1st and 3rd trimester is associated with serum adiponectin levels	MedDiet score assessed using 14-item questionnaire	Serum adiponectin levels	Age, pre-pregnancy BMI, gestational age, GWG, parity, education	From the first trimester to the third, concentrations of serum adiponectin decreased (-16% ± 4%, P=0.008), indicating increasing low-grade inflammation throughout pregnancy [26]. Though this study found support of diet attenuating this pattern, as women in the highest tertile of adherence to the MDS saw the lowest decrease in serum adiponectin (10% ± 11% vs. 34% ±3%, P=0.01)
Shin et al., 2017, U.S.	631 pregnant U.S. women from cross-sectional National Health and Nutrition Examination Survey (NHANES)	Examine association between pre-pregnancy BMI, DII and CRP during pregnancy	DII® from NHANES dietary questionnaire	CRP	Age, family poverty income ratio, race/ethnicity, education, marital status, smoking status, physical activity, parity	After controlling for confounders like race, SES, and smoking status, women who were classified as obese pre-pregnancy had increased odds for being in the highest tertile of DII and CRP concentrations compared to women of normal BMI pre-pregnancy (aOR=2.40, 95% CI: 1.01-5.71 for DII and aOR=24.84, 95% CI: 6.19-99.67 for CRP)

Pieczynska et al., 2020, Poland	Longitudinal study of 45 Polish pregnant women	To examine association between DII and IL-6, IL-10, and CRP	DII® score from seven-day 24-h recall and FFQ	IL-6, IL-10, and CRP	Pregnancy complications, age, education, place of residence, smoking status	Inflammation biomarkers were shown to increase with DII scores decreasing (meaning increasing overall dietary inflammation) from -1.78 in the first trimester to -2.71 in the third trimester, but this association was not significant (P=0.092)

HEI (Healthy Eating Index); SEIFA (Socioeconomic indices for areas disadvantage score); NICHD (National Institute of Child Health and Human Development); BMI (Body Mass Index); ASA-24 (Automated Self-Administered 24-recall); GWG (Gestational Weight Gain); IFPS II (Infant Feeding Practices Study II); WIC (Women, Infant, Child); AMED (Alternative Mediterranean Diet); AHEI (Alternative Healthy Eating Index); PPWR (Postpartum Weight Retention); hsCRP (highly sensitive C-Reactive Protein); SAA (Serum Amyloid A); IL- (Interleukin -) ; TNF-α (Tumor Necrosis Factor-alpha)

CHAPTER 3

METHODS

3.1 STUDY DESIGN AND POPULATION

In collaboration with the Centers for Disease Control (CDC), the Food and Drug Administration (FDA) conducted the Infant Feeding Practices Study (IFPS) II, a longitudinal study of women from late pregnancy through their infant's first year of life between 2005-2007 [60]. Survey topics included feeding practices, infant health, food allergies, sleeping arrangements, mother's employment, childcare, and mother's dietary intake[60]. The study sampled approximately 5,000 women from a nationally distributed consumer opinion panel of 500,000 households[60]. Study participants were excluded from the sample based on a birth screener that only qualified women and their infants if they did not have a medical condition at birth that would affect feeding, such as hypothyroidism. Infants also had to be born at least 35 weeks' gestation, have a birth weight of at least 5lbs, be a singleton, and have a stay of no more than 3 days if admitted to the neonatal intensive care unit. Data was collected once during pregnancy through a mailed questionnaire around the third trimester, once close to the time of birth through a phone interview, and after birth. After birth, 10 questionnaires were mailed during the 12-month postpartum period at approximately 2, 3, 4, 5, 6, 7, 10, and 12 months. In IFPS II, two dietary questionnaires were sent during late pregnancy and around 4 months postpartum. The IFPS II utilized a modified version of the National Cancer

Institute's (NCI's) Diet History Questionnaire (DHQ). The DHQ is a food frequency questionnaire (FFQ) that collects data on over 100 food items and portion size consumed. For the IFSP II study, the DHQ also collected data specific to pregnant and lactating women such as particular dietary supplements. The prenatal DHQ was mailed during the third trimester and represented dietary intake from week 28-36 of gestation and the postpartum DHQ was mailed and represented dietary intake between 3-4 months postpartum. The analysis for this study uses the postpartum DHQ to represent dietary intake between 3-4 months postpartum.

3.2 EXPOSURE OF INTEREST

The exposure in this study is the DII® score. The DII® is a literature-derived, population-based index that allows for the measurement of the inflammatory potential of an individual's diet[61]. A database compiled 1,943 peer-reviewed journal articles published through December 2010 evaluating links between 45 food parameters and the following markers of inflammation: IL-1β, IL-4, IL-6, IL-10, TNF-α, CRP. A total inflammatory effect (based on effect size of dietary parameter on inflammatory markers, the number of studies involving a specific food parameter, and the study design) for each parameter was determined by taking the difference of the anti-inflammatory effect from the pro-inflammatory effect and multiplying that value by the total weighted articles for that specific food parameter[61].

A complimentary database was also developed. This world composite database contains the global intake mean and standard deviation for each of the 45 food parameters based on data from 11 countries. Based on dietary intake for each food or nutrient parameter, an individual's intake of a specific parameter is expressed relative to a

standard global mean. This is done by subtracting the standard global mean from the amount reported by the individual and then divided by its standard deviation. Values are then converted into percentile scores to minimize the effect of 'right skewing'. Finally, each percentile score is doubled and then subtracted from 1 to achieve symmetrical distribution centered on 0 and with a range from -1 to 1. These centered percentiles are multiplied for each food parameter resulting in a final overall 'food parameter-specific inflammatory effect score'. After scoring each food or nutrient parameter in this manner, all parameters are summed to create an individual's overall DII® score. Thirty-seven of the total possible 45 food and nutrient parameters included in the DII® were collected from the DHQ in IFPS-II. Individual food and nutrient intakes were taken from the DHQ representing dietary quality at 3-4 months postpartum.

3.3 OUTCOME OF INTEREST

PPWR was calculated in kilograms by subtracting self-reported body weight at 3, 6, 9, and 12 months postpartum from the self-reported pre-pregnancy body weight. Pre-pregnancy body weight was self-reported on the prenatal questionnaire and subsequent body weights were self-reported in the 3, 6, 9, and 12-month postpartum questionnaires. The questionnaires were often not completed during the targeted time period and resulted in self-reported weights being collected between 11-73 weeks postpartum. Informed by previous research[55], postpartum time periods were redefined and categorized to provide equally spaced time intervals and reduce multiple measures of weight per woman per time interval. Time intervals used for this analysis were re-categorized to 11-20 weeks, 21-34 weeks, 35-48 weeks, and 49-62 weeks. A total 1,136 mothers had a self-reported pre-pregnancy weight and at least one postpartum weight. Twenty women were excluded

for implausible postpartum weights and 8 observations were excluded because they were collected after 62 weeks postpartum. In this analysis PPWR was first examined as a continuous variable and then dichotomized by substantial PPWR. Substantial PPWR (yes/no) was defined as retaining more than or equal to 4.55kg; this cut-off was determined based on recent literature[55].

3.4 COVARIATES

The following demographic variables were collected from the Panel Demographic Questionnaire or from a short supplement demographic questionnaire: maternal age, race/ethnicity, marital status (married/not married), parity (nulliparous/not), maternal education, geographical region, and poverty (yes/no). Race was categorized as non-Hispanic white, non-Hispanic black, Hispanic, and Asian/Pacific Islander/other. Geographical regions were condensed based on the US Census Bureau into Northeast, Midwest, South, and West. Education was defined as less than or equal to a high school diploma, some college, college graduate, or postgraduate. The US Census Bureau's 2006 poverty-threshold values were used to determine 185% of the federal poverty level cut off based on income and household size.

The following behavioral characteristics were included: smoking status (yes/no), alcohol (yes/no), breastfeeding duration (weeks), and breastfeeding (exclusively at least 6 or more months; yes/no). Smoking status was determined during pregnancy and the postpartum period. During pregnancy, smoking status was categorized as 'yes' if a mother responded to the survey with a value greater than zero for the average daily cigarettes smoked. During postpartum, smoking was assessed several times and subjects were classified as smokers if at any point during the follow up period they answered with

a value greater than 0 for average daily cigarettes smoked. Alcohol intake, measured through the DHQ questionnaire, was defined as yes/no in meeting the 2020 Dietary Guidelines for Americans recommendation of 1 or less standard alcohol drink per day for women. Study participants were asked to sum the total number of weeks they exclusively breastfed and the number of weeks they breastfed any amount in the last 12-month postpartum questionnaire. Breastfeeding was operationalized (yes/no) based on whether the infants were exclusively breastfed for 24 or more weeks. Breastfeeding was also measured by the total number of weeks mothers breastfed any amount.

Pre-pregnancy BMI and GWG were included as anthropometric measures. Pre-pregnancy BMI was categorized as normal (<25 kg/m^2), overweight (25 to < 30 kg/m^2), and obese (≥ 30 kg/m^2). GWG was defined based on the Institute of Medicine's (IOM) recommendations[62]. The IOM provides recommendations for appropriate weight gain during pregnancy based on pre-pregnancy BMI. IOM recommends that women gain no more than 25-35 lbs if their pre-pregnancy BMI was normal, no more than 15-25 lbs if their pre-pregnancy BMI was overweight, and no more than 11-20 lbs if their pre-pregnancy BMI was classified as obese. In this analysis, GWG was defined as within or outside (yes/no) the IOM's recommendations for GWG, by pre-pregnancy BMI.

3.5 STATISTICAL ANALYSIS

Pearson's chi-square analysis or ANOVA was used to identify and describe covariates significantly associated with DII® score quartiles and weight retention. A general estimating equations (GEE) model with an unstructured error term was used to determine the relationship between DII® scores and longitudinally measured PPWR. The odds of substantial PPWR (≥4.55 kg) at the end of the 12-month observation period was

evaluated for an association with DII® scores using a GEE model with an unstructured error term. The DII® score representing dietary intake from 3-4 months postpartum was collected at approximately the same time as the first measurement of PPWR between 11-20 weeks postpartum. Error terms were justified by comparing the QIC values of the full model with an exchangeable and unstructured error term for both the longitudinally measured PPWR and categorical substantial PPWR outcomes and confirmed by comparing the QIC values of the final models for each outcome. The following covariates were included in the models based on previous literature: age, education, race/ethnicity, marital status, poverty level, geographical region, smoking status, alcohol, breastfeeding duration, gestational weight gain, and pre-pregnancy BMI.

The final selection of covariates in both GEE models was determined using the backward elimination method to identify the possible predictors of both PPWR and substantial PPWR. At each step, variables were eliminated based on which covariate had the highest p-value. This process was repeated until all variables left in the model had a p-value less than 0.05. All results are represented with 95% confidence intervals and $P < 0.05$ from a two-sided significance test. Analyses were performed in RStudio (version 1.4.1103) using repeated measurement analysis, GEE procedures.

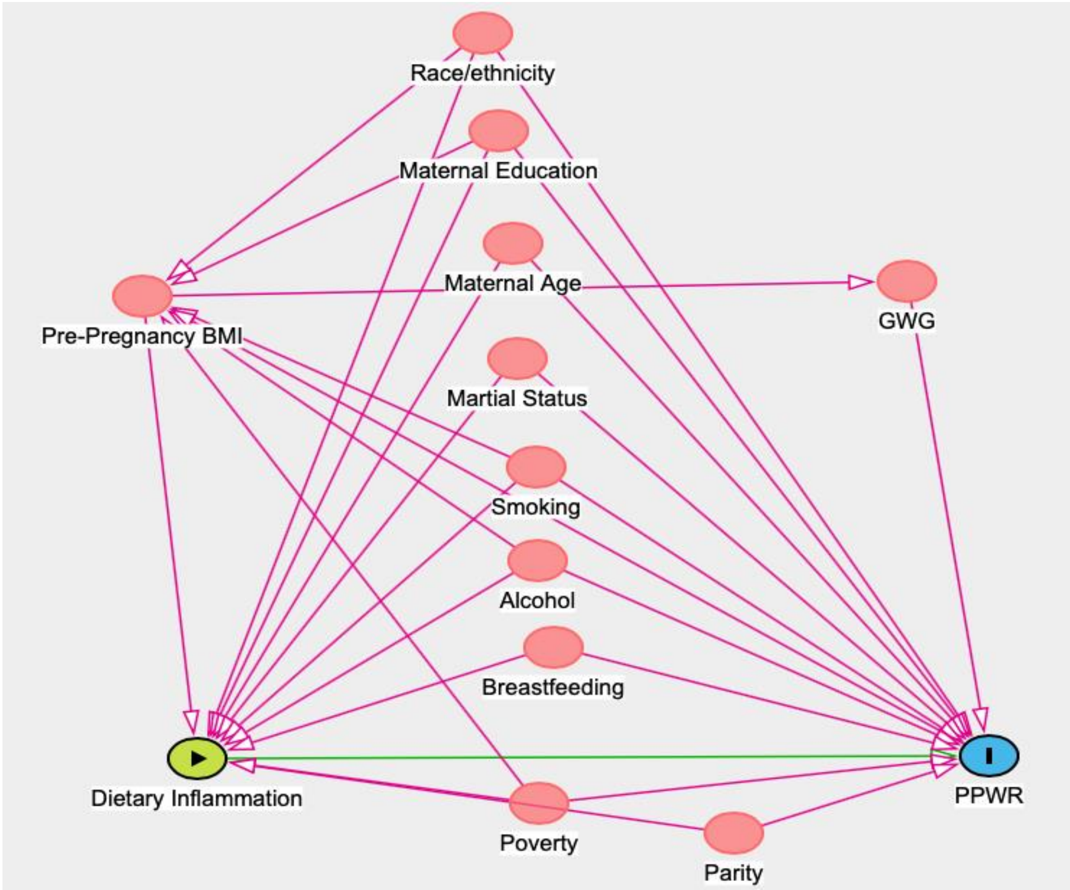

Figure 3.1 Directed Acyclic Graph (DAG)

CHAPTER 4

RESULTS

4.1 STUDY POPULATION

The final sample size included 1,136 women who had a recorded pre-pregnancy weight, completed the postpartum dietary questionnaire used to calculate the postpartum DII score, and had at least one self-reported postpartum weight measurement. The mean age of the sample was 29.2 years old with a standard deviation of 5.3 (**Table 4.1)**. The majority of women were non-Hispanic white (86%), fairly educated with some college or more (82.3%), married (82.7%), had previously given birth (70.2%), and lived above 185% of the Federal Poverty Level (FPL) (64.6%). The mean DII® score at 3-4 months postpartum was -0.80 with a standard deviation of 2.06. The mean weight retained at the end of the 62 weeks was 1.14 kg with a standard deviation of 6.70 kg. Twenty-two percent of women retained a substantial amount of weight (≥4.55 kg). Women with DII® scores in the highest quartile were more likely to have lower educational attainment, not be married, and living below 185% of the FPL (P<0.0001). Mothers with DII® scores in the highest quartile were also more likely to have smoked during or after pregnancy (P<0.0001), breastfed for less than 6 months (P<0.0001), and retained more than or equal to 4.55 kg of their GWG at weeks 11-20 (P=0.03) and weeks 35-48 (P=0.002).

4.2 PPWR

A linear relationship was observed between mean weight retained (kg) and time during the postpartum period (**Fig. 4.1**), confirming a linear relationship in the GEE model. Beginning with the full model (**Table 4.2**), through backwards elimination, with a p-value threshold of less than 0.05, DII® scores and the following covariates were eliminated from the full model: alcohol use, race/ethnicity, pre- and postnatal smoking status, breastfeeding at 6 months, and poverty status.

No significant association between DII® scores and postpartum weight retention (0.06 kg; 95% CI: [-0.11, 0.23]; P = 0.24) was detected (**Table 4.3**). Over the course of the follow up period significant weight loss occurred compared to the initial measurement at 11-20 weeks, with the greatest loss occurring at 35-48 weeks postpartum (-1.20 kg [95% CI: -1.50, -0.89 kg]). Being married (-1.37 kg; 95% CI: [-2.54, -0.20 kg]), nulliparous (-0.76 kg [95% CI: -1.50, -0.01 kg]), and breastfeeding for a longer duration (weeks) (-0.01 kg [95% CI: -0.02, -0.001 kg]) were significantly associated with lower PPWR at the end of the follow up period at 62 weeks. Women classified as overweight (-2.16 kg, [95% CI: -2.90, -2.43 kg]) and obese (-4.39 kg [95% CI: -5.37, -3.41 kg]) before pregnancy had greater weight loss at the end of the postpartum follow up period compared to women classified as having a Under or Normal pre-pregnancy BMI. Women retained significantly more weight if they had GWG less than (2.19 kg [95% CI: 1.27, 3.10 kg]) or greater than (5.59 kg [95% CI: 4.57, 6.61 kg]) IOM guidelines compared to women who had a GWG within IOM guidelines.

4.3 SUBSTAINTIAL PPWR

A negative quadratic relationship between the odds of substantial PPWR and DII® scores was inferred by plotting the probability of substantial PPWR and DII® scores

shown in **Fig. 4.2**. and the 'DII score^2' term was added to the full model. Starting with the full model (**Table 4.4**), through backwards elimination, with a p-value threshold of less than 0.05, the following covariates were eliminated from the full model: pre- and postnatal smoking status, poverty status, alcohol use, race/ethnicity, breastfeeding at 6mo, and age.

The final results from the reduced GEE model are shown in **Table 4.5**. No significant association between DII® scores and the odds of substantial PPWR at 12 months postpartum (OR: 1.03; 95% CI: [0.96, 1.10]; P = 0.24) was found. The odds of substantial PPWR were reduced over the follow up period compared to the initial weight measurement at 11-20 weeks, with the greatest reduction occurring at 35-48 weeks (OR: 0.63 [95% CI: 0.51, 0.75]) and 49-62 weeks (OR: 0.63 [95% CI: 0.51, 0.77]). Similar to the results seen with the continuous measure of PPWR, being married (OR: 0.64 [95% CI: 0.47, 0.90]), nulliparous (0.75 [95% CI: 0.58, 0.97]), and breastfeeding for a longer duration (weeks) (OR: 0.99 [95% CI: 0.991, 0.999]) were associated with reduced odds of substantial PPWR at the end of the follow up period. Reduced odds of substantial PPWR were also seen among women with an overweight (OR: 0.61 [95% CI: 0.46, 0.82]) or obese (OR: 0.51 [95% CI: 0.36, 0.71]) pre-pregnancy BMI as compared to women with an under or normal pre-pregnancy BMI. Women who had a GWG greater than the IOM guidelines (OR: 4.73 [95% CI: 3.19, 7.03]) had significant increased odds of substantial PPWR compared to women who had a GWG within the IOM guidelines.

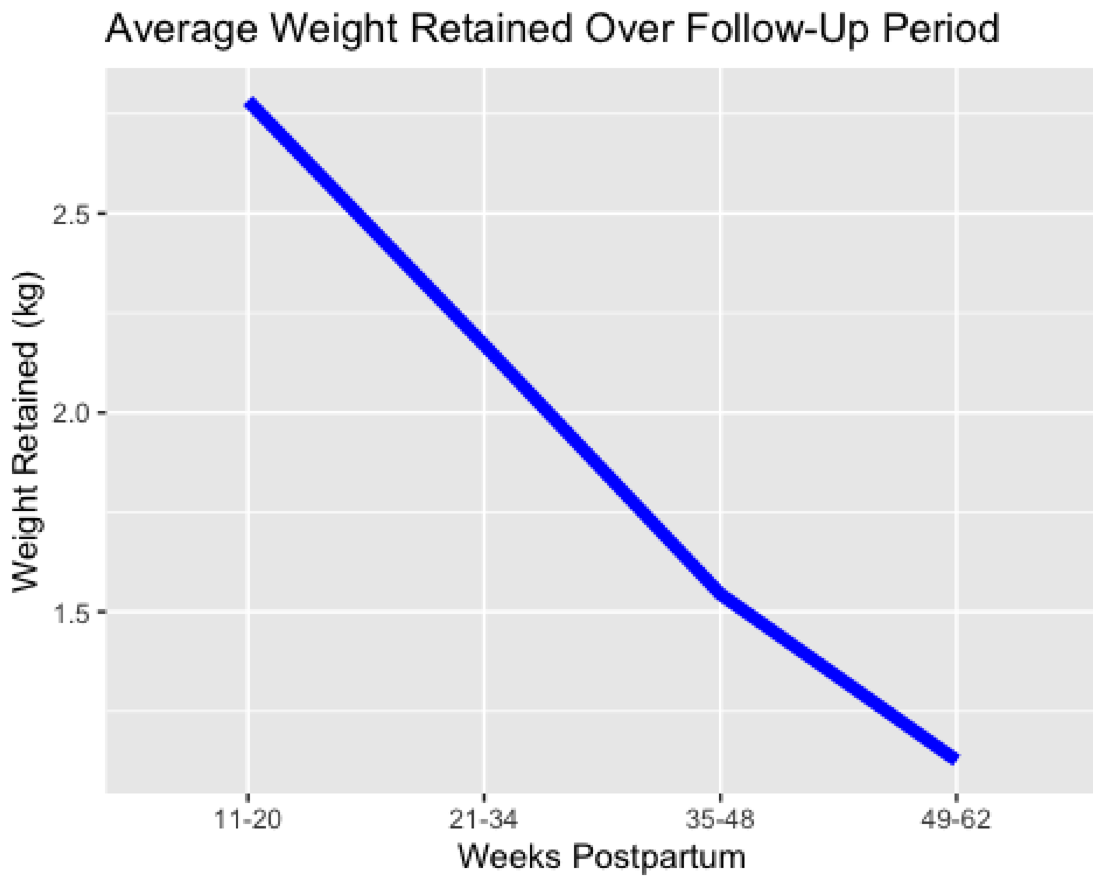

Figure 4.1 Average PPWR Over Follow Up Period

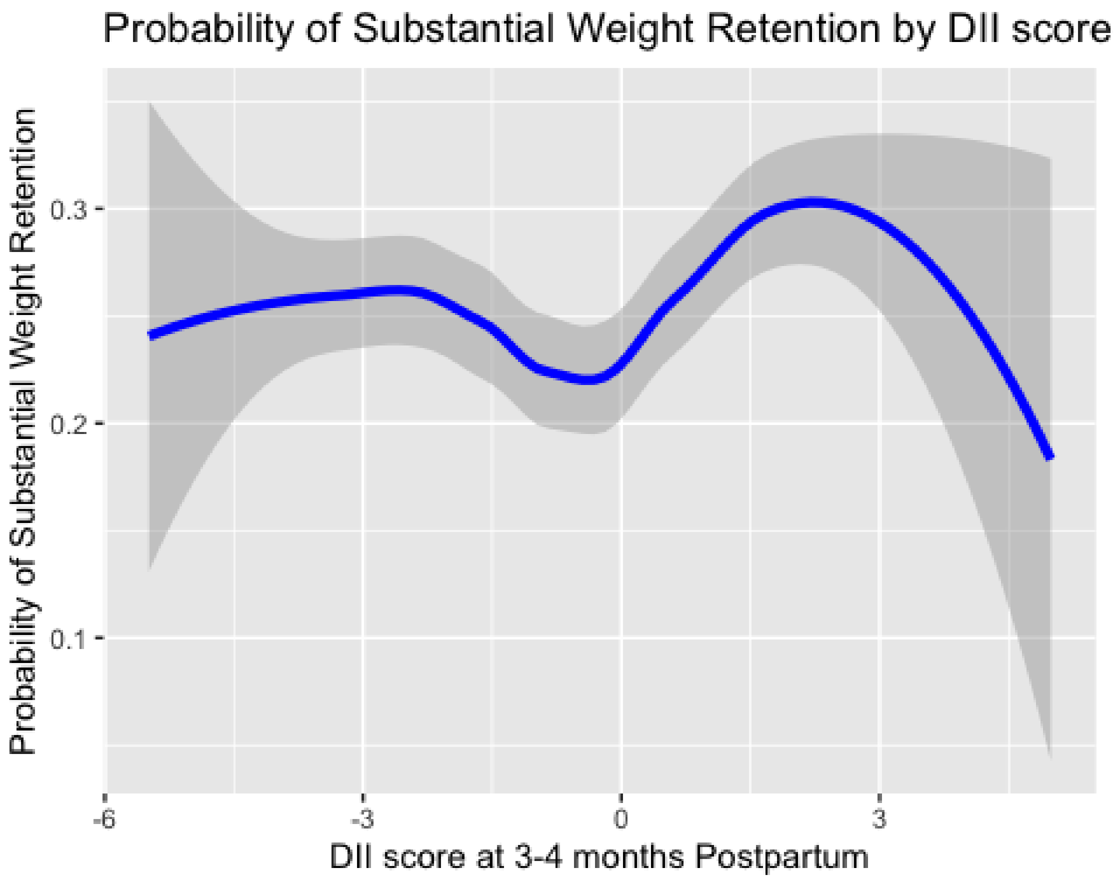

Figure 4.2 Probability of Substantial PPWR by DII® Score

Table 4.1 Maternal Characteristics by DII® Score Quartiles

	Total Cohort (n=1136)	**Q1 (≤-2.35; n=285)**	**Q2 (-2.36<x≤-0.80; n=283)**	**Q3 (-0.80<x≤0.66; n=284)**	**Q4 (>0.66; n=284)**	**P**
Demographics						
Age (y)	29.2 ± 5.3[2]	30.2 ± 5.4[2]	29.5 ± 5.1[2]	29.1 ± 5.2[2]	28.0 ± 5.1[2]	0.09
Education [n (%)]						**<0.0001**
High School or less	192 (17.7)	33 (12.3)	32 (11.9)	51 (18.2)	76 (27.5)	
Some college	411 (37.9)	84 (31.2)	90 (33.5)	113 (41.7)	124 (44.9)	
College graduate	358 (33.0)	106 (39.4)	108 (40.2)	79 (29.2)	65 (23.6)	
Graduate degree	124 (11.4)	46 (17.1)	39 (14.5)	28 (10.3)	11 (4.0)	
Race/ethnicity [n (%)]						0.09
Non-Hispanic white	963 (86.0)	277 (81.4)	242 (86.1)	247 (87.3)	247 (89.2)	
Non-Hispanic black	39 (3.5)	9 (3.2)	9 (3.2)	8 (2.8)	13 (4.7)	

Hispanic	58 (5.2)	19 (6.8)	15 (5.3)	14 (5.0)	10 (3.6)	
Asian/Pacific Islander/other	60 (5.4)	24 (8.6)	15 (5.3)	14 (5.0)	7 (2.5)	
Married [n (%)]	8986 (82.7)	253 (21.7)	231 (21.3)	229 (21.1)	201 (18.6)	**<0.0001**
Poverty level (<185% of federal poverty level) [n (%)]	402 (35.4)	65 (5.7)	87 (7.7)	110 (9.7)	140 (12.3)	**<0.0001**
Nulliparous [n (%)]	331(29.8)	93 (8.4)	75 (6.8)	84 (7.6)	79 (7.1)	0.40
Behavioral Characteristics						
Smoked during pregnancy [n (%)]	89 (7.9)	13 (1.1)	9 (0.8)	21 (1.9)	46 (4.1)	**<0.0001**
Smoked postpartum [n (%)]	175 (16.6)	27 (2.6)	27 (2.6)	40 (3.8)	81 (7.7)	**<0.0001**
Alcohol [n (%)] (not meet US Guidelines)	32 (2.8)	10 (0.9)	4 (0.4)	8 (0.7)	10 (0.8)	0.38
Breastfeeding duration (weeks) [n]	35.2 ± 30.6	40.6 ± 31.0	39.4 ± 31.3	34.4 ± 29.2	26.2 ± 28.9	**0.04**
Breastfeeding 6 months or more [n (%)]	563 (49.6)	164 (14.4)	156 (13.7)	137 (12.1)	106 (9.3)	**<0.0001**
Anthropometric measures						

Pre-pregnancy BMI [n (%)]						0.07
<25 kg/m^2	598 (52.7)	165 (58.1)	160 (56.5)	139 (48.9)	134 (47.4)	
25 to <30 kg/m^2	284 (25.0)	69 (24.3)	63 (22.3)	77 (27.1)	75 (26.5)	
≥30 kg/m^2	252 (22.2)	50 (17.6)	60 (21.2)	68 (23.9)	74 (26.2)	
Gestational weight gain [n (%)]						0.11
Less than IOM guidelines	205 (18.1)	42 (14.8)	44 (15.6)	55 (19.4)	64 (22.6)	
Within IOM guidelines	418 (36.9)	110 (38.7)	117 (41.3)	100 (35.2)	91 (32.2)	
Greater than IOM guidelines	511 (45.1)	132 (46.5)	122 (43.1)	129 (45.2)	128 (45.2)	
Weight retention ≥ 4.55 kg [n (%)]						
11-20 weeks	324 (31.2)	100 (9.6)	71 (6.8)	69 (6.7)	84 (8.1)	**0.03**
21-34 weeks	240 (25.3)	63 (6.6)	57 (6.0)	50 (5.7)	70 (7.4)	0.21
35-48 weeks	203 (22.9)	42 (4.7)	51 (5.7)	41 (4.6)	69 (7.8)	**0.0002**
49-62 weeks	182 (22.4)	41 (5.1)	49 (6.0)	41 (5.1)	51 (6.3)	0.28

Table 4.2 Full GEE Model Examining Factors Associated with PPWR

	Full Model
Variable	Weight Retention (kg)
(Intercept)	1.91
DII® Score	0.04
Weeks Postpartum	
11-20 weeks	Ref.
21-34 weeks	-0.65***
35-48 weeks	-1.21***
49-62 weeks	-1.63***
Education	
<High School	Ref.
Some College	-0.97*
College graduate	-1.00*
Graduate degree	-1.25*
Race/Ethnicity	
NH-white	Ref.
NH-black	1.55
Hispanic	0.05
API/Other	-0.61
Married	-1.37*
<185% of FPL	-0.50
Nulliparous	0.11*
Does not meet US guidelines for Alcohol consumption (postpartum)	0.11
Breastfeeding at 6 months	0.30
Weeks of breastfeeding	-0.02*
Smoked during pregnancy	-0.29
Smoked during postpartum	-0.69
Pre-pregnancy BMI	
Under & Normal	Ref.
Overweight	-2.04***
Obese	-4.13***

Gestational Weight Gain	
Within IOM guidelines	Ref.
Less than IOM guidelines	2.34***
Greater than IOM guidelines	5.80***
Age	0.08*

* p-value less than 0.05 ** p-value less than or equal to 0.01 ***p-value less than 0.0001

Table 4.3 Final GEE Model Examining Factors Associated with PPWR after Backwards Elimination

Variable	Weight Retention (kg) [95% CI]	P-value
(Intercept)	2.01 [-0.36, 4.38]	0.05
DII® Score	0.06 [-0.11, 0.23]	0.24
Weeks Postpartum		
11-20 weeks	Ref.	
21-34 weeks	-0.67 [-0.91, -0.43]	<0.0001
35-48 weeks	-1.20 [-1.50, -0.89]	<0.0001
49-62 weeks	-0.64 [-2.04, -1.25]	<0.0001
Education		
<High School	Ref.	
Some College	-0.76 [-1.85, 0.33]	0.09
College graduate	-1.04 [-2.10, 0.02]	0.03
Graduate degree	-1.06 [-2.35, 0.23]	0.05
Married	-1.37 [-2.54, -0.20]	0.01
Nulliparous	-0.76 [-1.50, -0.01]	0.02
Weeks of breastfeeding	-0.01 [-0.02, -0.001]	0.02
Pre-pregnancy BMI		
Under & Normal	Ref.	
Overweight	-2.16 [-2.90, -2.43]	<0.0001
Obese	-4.39 [-5.37, -3.41]	<0.0001
Gestational Weight Gain		
Within IOM guidelines	Ref.	
Less than IOM guidelines	2.19 [1.27, 3.10]	<0.0001
Greater than IOM guidelines	5.59 [4.57, 6.61]	<0.0001
Age	0.06 [-0.01, 0.14]	0.05

Table 4.4 Full GEE Model Examining Factors Associated with Odds of Substantial PPWR (≥4.55 kg)

Odds of Substantial Weight Retention (kg)	
Variable	Full Model
(Intercept)	0.48
DII® Score	1.02
DII® Score^2	0.98
Weeks Postpartum	
11-20 weeks	Ref.
21-34 weeks	0.71***
35-48 weeks	0.63***
49-62 weeks	0.63***
Education	
<High School	Ref.
Some College	0.85
College graduate	0.70
Graduate degree	0.73
Race/Ethnicity	
NH-white	Ref.
NH-black	1.12
Hispanic	1.07
API/Other	0.75
Married	0.67 **
<185% of FPL	0.92
Nulliparous	0.73 *
Does not meet US guidelines for Alcohol consumption (postpartum)	0.95
Breastfeeding at 6 months	1.24
Weeks of breastfeeding	0.99*
Smoked during pregnancy	1.07
Smoked during postpartum	1.02
Pre-pregnancy BMI	
Under & Normal	Ref.
Overweight	0.60***

Obese	0.55***
Gestational Weight Gain	
Within IOM guidelines	Ref.
Less than IOM guidelines	1.32
Greater than IOM guidelines	4.88***
Age	1.01

* p-value less than 0.05   ** p-value less than or equal to 0.01   ***p-value less than 0.0001

Table 4.5 Final GEE Model Examining Factors Associated with Odds of Substantial PPWR (≥4.55kg) after Backwards Elimination

Variable	Odds of Substantial Weight Retention (≥4.55 kg) [95% CI]	P-value
(Intercept)	0.58 [0.34, 0.98]	0.02
DII Score	1.03 [0.96, 1.10]	0.24
DII Score^2	0.99 [0.96, 1.01]	0.10
Weeks Postpartum		
11-20 weeks	Ref.	
21-34 weeks	0.70 [0.61, 0.81]	<0.0001
35-48 weeks	0.63 [0.52, 0.75]	<0.0001
49-62 weeks	0.63 [0.51, 0.77]	<0.0001
Education		
<High School	Ref.	
Some College	0.88 [0.63, 1.23]	0.22
College graduate	0.67 [0.46, 0.98]	0.02
Graduate degree	0.74 [0.46, 1.17]	0.10
Married	0.65 [0.47, 0.90]	0.004
Nulliparous	0.75 [0.58, 0.97]	0.01
Weeks of breastfeeding	0.99 [0.991, 0.999]	0.01
Pre-pregnancy BMI		
Under & Normal	Ref.	
Overweight	0.61 [0.46, 0.82]	0.0005
Obese	0.51 [0.36, 0.71]	<0.0001
Gestational Weight Gain		
Within IOM guidelines	Ref.	
Less than IOM guidelines	1.25 [0.82, 1.89]	0.15
Greater than IOM guidelines	4.73 [3.19, 7.03]	<0.0001

CHAPTER 5

DISCUSSION

5.1 SUMMARY OF RESULTS

The objective of this study was to examine the relationship between the inflammatory potential of women's diet, measured by the DII®, at 3-4 months postpartum and weight retained during the postpartum period. This secondary analysis found no significant association between the DII® score and postpartum weight retention nor any significant association with odds of substantial PPWR at 12 months postpartum. The study did find a significant relationship between PPWR and substantial PPWR with other covariates included in the model. Longer time since delivery, being married, nulliparous, longer breastfeeding duration, and having an overweight/obese pre-pregnancy BMI were all significantly associated with lower PPWR. Women with GWG outside the IOM's recommendations had increased PPWR at 12 months. Similar results were seen with the odds of substantial PPWR. Longer time since delivery, being married, nulliparous, longer breastfeeding duration, and an overweight/obese pre-pregnancy BMI reduced the odds of substantial PPWR, while women who gained gestational weight outside of IOM's recommendations had increased odds of PPWR.

5.2 INTERPRETATIONS AND IMPLICATIONS

Entering pregnancy overweight/obese can put mothers and their children at an increased risk for adverse maternal and birth outcomes[1–5]. Retaining weight from

pregnancy and entering a subsequent pregnancy at an overweight or obese BMI puts women at an increased risk for hypertensive disorders, GDM, cesarean delivery, and preterm birth[1–4]. It also increases the risk of women developing type 2 diabetes and cardiovascular disease after birth[2,3]. At the end of the follow up period in this study, women retained an average of 1.1 kg (SD: ± 6.7 kg), but 22% of mothers had substantial PPWR (≥4.55 kg). Among those 22% of mothers with substantial PPWR at 12 months postpartum, the median PPWR was 9 kg or approximately 20 lbs. PPWR contributes to obesity after childbirth, but can also be a potential window of time for intervention and prevention through diet [1,5].

Compared to the other studies within our review considering the relationship between diet quality during and after pregnancy and PPWR[18,19,55], some differences that might have influenced our null results. These differences stem from the timing of the diet quality measure, differences in study population characteristics, and the inclusion or exclusion of additional measures, such as sleep, inflammation, and physical activity. All of the three studies reviewing the relationship between diet quality and PPWR, did find evidence that support the importance of the quantity of food consumption over diet quality in regards to losing weight after pregnancy.

Overall, there is little information about how diet quality changes over the course of pregnancy[15]. There is an upward trend of more women entering into pregnancy at an overweight or obese BMI[2]. The literature review yielded studies that provided initial evidence that diet quality in pregnancy does not meet recommendations for women, and that diet quality may even further decrease in the postpartum period[15,29,37]. Three studies within this literature review examined diet quality and PPWR[18,19,55]. Loy examined how

diet quality impacts PPWR and measured diet quality using HEI scores at 26-28 weeks gestation[18]. Loy et al.'s study was able to detect a relationship between their measures of diet quality during the prenatal period and PPWR with higher quality diet leading to reductions in PPWR. Boghossian and Stendell-Hollis both measured diet quality at 4 months postpartum using MDS[19,55]. Both studies had an average MDS score of 4, or moderate at the baseline measurement[19,55]. Boghossian was not able to find evidence of MDS scores impacting PPWR nor substantial PPWR (≥4.55 kg) at 12 months[55]. Stendell-Hollis, measuring the impact of a dietary intervention found that the intervention did not lead to significant changes in MDS scores but did lead to a small, significant reduction in PPWR[19]. Our study added to the literature by describing diet quality during the postpartum period, using the DII score, measuring the dietary inflammatory potential of diet. At 3-4 months postpartum the average and median DII score in the study sample was -0.797 and -0.795, respectfully, and the scores ranged between -5.49 and 4.99. Though no association was found between DII® scores and PPWR.

Study population characteristics differences could also be a source that might explain our study's null results. From the literature review, Enders et al. identified race, age, income/poverty, education, and insurance status to be risk factors for women retaining at least 20lbs, 1 year after birth[5]. Boghossian and this study utilized the same population from the Infant Feeding Practices Study II. This and Boghossian's study population consisted of mostly white women, who had some college or had obtained a degree, were married, had pervious given birth, and lived above 185% of the FPL[55]. Both analysis found that neither DII, AHEI, nor MED had an influence on PPWR[55]. Loy et al. showed reduced odds of substantial PPWR from a high quality diet, evaluated by HEI,

after 8 months postpartum[18] among, women living Singapore. Though other than ethnicity, both Boghossian and this study's population of women were similar to Loy's study population in regards to age, education, parity, socioeconomic status, and pre-pregnancy BMI[18,19,55]. Stendell-Hollis found that after comparing adherence to the USDA's MyPyramid or the MDS diets, adherence to both led to significant reductions in PPWR, with no discernable differences between the diets[19]. Stendell-Hollis study occurred among 129 overweight women, where among this study sample 52.7% of women had a pre-pregnancy BMI of Normal or Under. Stendell-Hollis study population was also made up of women, whom the majority of were exclusively breastfeeding in conjunction with the dietary intervention[19].

The results of this study did provide further evidence for the importance of other factors in association with PPWR. While no association was detected between DII® scores and PPWR; GWG, parity, breastfeeding duration, and pre-pregnancy BMI were significantly associated with PPWR, similar to previous studies[6]. Using different measurements for breastfeeding, Boghossian and this secondary analysis found it to be a significant predictor of PPWR and Stendell-Hollis found significant reductions in body weight after a diet intervention among women exclusively breastfeeding.

There are also other factors, such sleep, physical activity, and inflammation, that this analysis did not measured, were included in others. Loy measured physical activity as MET minutes per week and sleep duration and found neither were significant predictors of substantial PPWR (≥5 kg). The DII® score, while has been strongly correlated with measures of individual inflammation markers in the general population[57,58], is not a proxy measure for inflammation. The DII® score measures the

inflammatory potential of an individual's diet and this study found no association with PPWR. Stendell-Hollis measured two individual biomarkers associated with inflammation, TNF-α and IL-6, before and after the study's diet intervention and found a decrease in TNF-α for both the MDS and MyPyramid diet intervention groups. No significant change was observed for the levels of IL-6, and this study did not measure the effect of individual inflammation biomarkers on PPWR.

A deeper understanding is also needed on how pre-pregnancy BMI, GWG, and PPWR all influence each other and what role diet quality plays. Parker and colleagues observed an inverse relationship for both GWG and pre-pregnancy BMI with diet quality, measured by AHEI within the Infant Feeding Practices Study II,[51] though this relationship was modified by pre-pregnancy BMI. Pre-pregnancy BMI could also modify the association between diet quality and PPWR.

The results from this study taken in context of previous research provide evidence that support the claim that diet quality might have a little to no impact on PPWR. Total energy/caloric intake or food group consumption might have a larger impact on postpartum weight loss. For the two studies that found significant relationship between diet quality (MDS and HEI) and PPWR also included measures total caloric intake, timing of eating, and food group intakes[18,19]. Stendell-Hollis study participants in both the MDS and MyPyramid dietary intervention demonstrated significant reductions in total energy intake (MDS: -251.2 kcal/day, P=0.045; MyPyramid: -437.5 kcal/day, P=0.003)[19]. Loy also found that greater caloric intake at night during the prenatal period to be independently associated with higher odds of substantial PPWR (>5 kg)[18]. Boghossian, who did not find a significant association between AHEI and MDS with PPWR, also

measured total energy intake in kcal and macronutrients. Boghossian's study found that PPWR and substantial PPWR were associated with total energy intake at 7-14 months postpartum (PPWR: 0.97 kg/1000 kcal; 95% CI: 0.40, 1.55 kg/1000 kcal) (OR substantial PPWR: 1.25/1000 kcal; 95% CI: 1.03, 1.52 /1000 kacal)[55].

5.3 STRENGHTS AND LIMITATIONS

The current study has several strengths but should be interpreted in light of its limitations. The study set out to examine the association between diet quality, measured using the DII® score, and PPWR. The objective of this study was unique with a novel use of DII scores among postpartum women investigating the effect on PPWR. Our literature review resulted in only three studies examining the association between diet quality and PPWR and no previous studies between 2010 and July 2021 had examined the association between diet quality, measured using the DII® score, and PPWR. We conducted our analyses using data from the Infant Feeding Practices Study II, a national, longitudinal survey following mothers and their infants from pregnancy until the infant's first birthday. Using this data resulted in a large sample size of 1,136 mothers, with a retention rate of 71% at the end of the follow up period. The longitudinal data and the availability of data on multiple covariates, including behavioral, socioeconomic, and anthropometric variables, added to the strength of this study's results.

The generalizability of our findings is limited because the sample is not representative of the national population of the United States. Our sample size was 86% white compared to the national percentage of 57.8% from the 2020 census[63], restricting how applicable the results are to other ethnic and racial groups. Our study population was also more educated (44.4% vs 32.9%) with at least a bachelor's degree[64]. All weights

were self-reported by the mothers and that introduces the potential for measurement bias. Additionally, participants might be susceptible to recall bias when reporting their pre-pregnancy weight during the prenatal period. Our models included several covariates that have been previously reported to be associated with diet and PPWR. However, our analysis did not include a measure for physical activity, sleep, and individual inflammation biomarkers.

There are also limitations in the approach of the analysis. For both the continuous measure of PPWR and the odds of substantial PPWR using GEE model, a backwards elimination approach was taken in selecting variables for the final models. There are limitations with a backward elimination selection. A backwards elimination selection allows for the assessment for the joint predictive ability of variables, but weakness of the this selection methods is once a variable is eliminated from the model it cannot be reentered[65].

5.4 FUTURE STUDIES

Current epidemiological research does not offer conclusive results on the relationship between diet quality and PPWR. From this study's literature review, there is evidence that diet quality does not meet recommendations for women and that diet quality does not improve or even worsens after birth[15,29,37]. Future studies examining DII® scores and PPWR should continue using a longitudinal study design, but asses DII scores before, during, and after pregnancy. Pre-pregnancy BMI should be analyzed as an effect modifier between DII® scores and PPWR to gain a deeper understanding on how pre-pregnancy BMI, GWG, and PPWR all influence each other when evaluating the

impact of diet quality. Consideration should also be taken to focus future study's population among women who enter pregnancy overweight/obese.

This study's null results also call into question the importance of diet quality when trying to reduce PPWR. In studies that have examined diet quality and PPWR, whether the results were significant or not, a third variable, total caloric intake, remains a significant predictor. Future studies should directly compare if improving diet quality or reducing caloric intake has a larger impact on PPWR.

5.5 CONCLUSION

This study did not find evidence that DII scores are associated with mean PPWR nor the odds of substantial PPWR. Time after delivery, marital status, parity, breastfeeding duration, pre-pregnancy BMI, and GWG were all significant covariates with PPWR and substantial PPWR. This study is novel and adds to the literature assessing DII scores and PPWR, but more research is needed to assess the importance of DII on PPWR reduction.

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