

# Association of Milk and Dairy Products Consumption During Pregnancy with Fetal and Neonatal Head Circumferences: A Systematic Review

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## Abstract

**Context:** Milk and dairy products consumed by mothers seem to be effective for fetal and neonatal anthropometric measurements, because they contain various nutrients.

**Objectives:** The aim of this study was to systematically review the influence of milk and dairy products consumption by mothers on fetal and neonatal head circumferences.

**Data Sources:** Systematic searches were conducted in electronic databases including PubMed/MEDLINE, Scopus, ISI, Ovid, Embase, Medlib, Google Scholar, clinical trials and Cochrane central register of clinical trials.

**Study Selection:** All studies that assessed the relationship between milk and dairy products consumption in healthy females during pregnancy and fetal and neonatal head circumferences were included in our systematic review. Finally, seven studies were relevant that included five cohort studies, one cross-sectional study and one randomized clinical trial.

**Data Extraction:** This systematic review was performed based on the preferred reporting item for systematic reviews and meta-analysis (PRISMA) statement recommendation, and for quality assessment, the Newcastle-Ottawa scale (NOS) for cohort studies, the adapted NOS for a cross-sectional study and the Jadad quality assessment score for a randomized clinical trial, were used.

**Results:** Seven studies that comprised of more than 50000 pregnant females were included in this review. One cohort study, one cross-sectional study and one randomized controlled trial study showed that milk or dairy products consumption by pregnant mothers was not associated with neonatal birth head circumference, while three cohort studies reported that maternal milk or dairy products intake had a positive effect on neonatal birth head circumference. Two cohort studies showed that there was no relationship between maternal milk or dairy products consumption and fetal head circumference while a cross-sectional study reported that there was a positive relationship between milk or dairy products consumption during pregnancy and fetal head circumference.

**Conclusions:** Evidences in this field are limited and inconsistent. According to the findings, there is a positive association between milk and dairy products consumption by pregnant mothers and neonatal birth head circumference but there is no relationship between maternal milk and dairy products consumption and fetal head circumference. However, almost all studies emphasized the importance of milk and dairy products in the maternal diet as a source of valuable nutrients.

**Keywords:** Milk, Dairy Products, Maternal Nutrition, Fetal Head Circumference, Neonatal Birth Head Circumference, Systematic Review

## 1. Context

Pregnancy is one of the most critical and important periods in a female's life. Due to higher nutritional requirements during pregnancy, pregnant females are considered vulnerable and at risk in life span (1). Thus, maternal diet must provide sufficient energy and nutrients to meet the mother's usual requirements, as well as the needs of the growing fetus and enable the mother to provide stores of nutrients required for fetal development (2). Maternal nu-

trition is one of the major environmental factors that influences fetal growth and neonatal birth size (3, 4). Anthropometric measurements at birth are important predictors of neonatal morbidity and mortality (5). The reviewed studies showed that thinness and small head circumference at birth had an association with death from cardiovascular disease during adult life (6-8) and a retrospective cohort study in China reported that smaller head circumference at birth could predict worse adulthood quality of life (QOL)

at above 50 years old (9). Thus, investigation of dietary intake is an important part of pregnancy and birth studies.

Nowadays, the focus is shifting from assessment of the impact of single dietary nutrients to studying food groups and dietary patterns in relation to pregnancy outcomes (10). Among food groups, milk and dairy products are more effective for fetal growth and neonatal birth size because they contain various nutrients such as protein, calcium, phosphorus, potassium, iodine, vitamin B12 and riboflavin (11). However, the findings are inconsistent and did not provide a clear conclusion; three studies, one cohort study, one cross-sectional study and one randomized controlled trial (12-14), showed that maternal milk or dairy products intake were not associated with neonatal birth head circumference, while three cohort studies (15-17) reported that maternal milk or dairy products consumption had a positive effect on neonatal birth head circumference. Two cohort studies (16, 18) showed that there was no relationship between maternal milk or dairy products intake and fetal head circumference while a cross-sectional study (13) reported that there was a positive relationship between milk or dairy products consumption during pregnancy and fetal head circumference.

## 2. Objectives

The aim of this systematic literature review was to assess the influence of maternal milk and dairy products consumption during pregnancy on fetal and neonatal head circumferences.

## 3. Data Sources

Systematic literature searches were conducted in international databases including: PubMed/MEDLINE, Scopus, ISI, Ovid, Embase, Medlib, Google Scholar, clinical trials and Cochrane central register of clinical trials, without any restriction for type, time and language to identify the relevant literature.

The following medical subject headings and keywords were used to search all fields in the above databases from April to May 2015, ("Milk" OR "Milk Products" OR "Dairy" OR "Dairy Products" OR "Cultured Milk Products") AND ("Eating" OR "Intake" OR "Consumption" OR "Drinking") AND ("Pregnancy" OR "Pregnant" OR "Gestation") AND "Head Circumference". An additional manual search was performed using reference lists from the research studies and review articles to identify other eligible studies.

The present systematic review was performed based on the preferred reporting item for systematic reviews and meta-analysis (PRISMA) statement recommendation and has been registered by PROSPERO (ID = CRD42015020191).

## 4. Study Selection

Duplicated, irrelevant and non-human subject studies were excluded. Two researchers retrieved full-text of the remaining studies for further examination. Any disagreement on study selection were resolved by the third investigator.

The Newcastle-Ottawa scale (NOS) for five cohort studies, the adapted NOS for one cross-sectional study (19) and the Jadad et al. (20) quality assessment score for one randomized clinical trial were used to assess the methodological quality of the included studies. The NOS, 'a star system' is based on three board perspectives: the selection of the study groups, the comparability of the groups, and the ascertainment of either the exposure or outcome. The Jadad is based on three aspects: randomization, blinding and withdrawals. Two investigators assessed the quality of the studies according to the above scales.

## 5. Data Extraction

A total of 1560 studies were initially identified in the databases. After excluding duplicate studies, 664 articles were retrieved and we reviewed them based on their titles and abstracts; 66 articles were selected for a more detailed review.

Fifty-nine articles were excluded because of the following reasons: 50 articles did not report on consumption of milk and dairy products for pregnant mothers or fetal/birth head circumferences among their outcomes. Five studies focused on non-human subjects and four studies provided data for fortified milk or dairy products with completely different composition from current milk or dairy products (Figure 1).

Data extracted from selected studies, included: first author, study design, country, sample size, duration of studies, age of participants, milk or dairy products consumption, head circumference as an outcome, confounder adjustment, quality, method of dietary assessment and time period covered dietary intake, average and range of milk or dairy products consumption and results (Tables 1 and 2).

### 5.1. Risk of Bias in Individual Studies

Articles were selected and appraised for risk of bias by two independent reviewers. The assessment of risk of bias was performed separately for each study design. We used the Cochrane risk of bias tool, Newcastle Ottawa quality appraisal tool and strengthening the reporting of observational studies in epidemiology (STROBE) checklist. All studies had a low risk of bias.

## 6. Results

Seven studies were included in this review (Figure 1) that included five cohort studies, one cross-sectional study and one randomized clinical trial. A total of more than 50000 pregnant women were included in our review, of which 87% were from Denmark and Netherlands, 12% were from India and 1% was from USA and Canada (Table 1).

The dietary assessment, time of administration, time period covered and milk or dairy products intake range differed between the studies (Table 2). Studies reported milk or dairy products intake by volume, servings or frequencies of intake. However, a direct comparison of the average daily consumption of milk or dairy products was not possible because of the lack of information in some of the studies (Table 2).

Quality assessment score of studies is shown in Table 1. The main biases in cohort studies related to their outcome of interest were not present at start of the study and non-blinding for a randomized clinical trial.

Among the seven studies, four studies reported results of maternal milk or dairy products consumption in relation to neonatal birth head circumference (12, 14, 15, 17), one study reported results of maternal milk or dairy products consumption in relation to fetal head circumference (18) and two studies reported results of maternal milk or dairy products consumption in relation to both fetal and neonatal birth head circumferences (13, 16).

One cohort study, one cross-sectional study and one randomized controlled trial (12-14) showed that maternal milk or dairy products consumption was not associated with neonatal birth head circumference, while three cohort studies (15-17) reported that maternal milk or dairy products intake had a positive effect on neonatal birth head circumference.

Two cohort studies (16, 18) showed that there was no relationship between maternal milk or dairy products consumption and fetal head intake while a cross-sectional study (13) reported that there was a positive relationship between milk or dairy products intake during pregnancy and fetal head circumference.

Mannion et al. (12) reported that neonatal birth head circumference in females, who consumed  $\leq 250$  mL/d of milk in comparison with higher consumption were similar. In addition, Borazjani (13) found no association between maternal milk consumption during pregnancy and neonatal birth head circumference. The respondents were met in the last trimester of pregnancy and the majority were met during the last month of pregnancy, close to delivery time, and milk consumption (mL/d) was assessed in 5 categories (Cup  $\approx 150$  mL; None,  $< 150$  mL/d, 150 - 300 mL/d, 300 - 450 mL/d and  $> 450$  mL/d). Potdar et

al. (14) assessed the daily portion of food that contained green leafy vegetables, fruit and milk powder on birth measurement including neonatal birth head circumference. Snacks were made from approximately 14 g commercially-bought full-fat milk powder. Participants were given one snack/day from 90 days before the last menstrual period date until delivery. The findings showed no significant association between intakes of snack containing milk powder and neonatal birth head circumference. While, Olsen et al. (15) reported that consumption of milk  $> 6$  glass/d (glass  $\approx 200$  mL) during 21 - 25 weeks in pregnancy increased (95% CI: 0.04 - 0.25 cm) the mean of neonatal birth head circumference by 0.13 cm, after adjustment for confounders, including: infants gender, mother's parity, age, height, pre-pregnancy BMI, gestational weight gain, smoking status, total energy intake, father's height and family's socioeconomic status in the large Danish national birth cohort (DNBC). Heppel et al. (16) reported that first-trimester maternal milk consumption of  $> 2 - 3$  glasses/day (glass  $\approx 150$  mL) was associated with 2.2-cm larger head circumference at birth (P for trend = 0.03). Rao et al. (17) showed that the frequency of milk consumption at 18-week gestation was related to neonatal birth head circumference in the Pune maternal nutrition cohort study, Maharashtra, India. Heppel et al. (16) found no consistent associations of first-trimester maternal milk consumption with fetal head circumference. In addition, Chang et al. (18) showed no significant associations of serving dairy intake (one serving  $\approx 1$  glass  $\approx 260$  mL milk) that was estimated at first prenatal visit with fetal head circumference (P for trend = 0.713), in addition no significant relationships were found between fetal head circumference, by using the regression model, which corrected for fetal biparietal diameter, and maternal dairy intake. Borazjani (13) reported that there was a positive contribution between maternal milk intake and fetal head circumference.

## 7. Discussion

Studies assessed the association between maternal milk and dairy products intake on neonatal birth head circumference or fetal head circumference. In this systematic literature review, one cohort study (12), one cross-sectional study (13) and one randomized controlled trial study (14) declared that maternal milk or dairy products consumption were not associated with neonatal birth head circumference, while three cohort studies (15-17) reported that maternal milk or dairy products consumption had a positive effect on neonatal birth head circumference. Two cohort studies (16, 18) showed that there was no relationship between maternal milk or dairy products intake and fetal head circumference while one cross-sectional study (13)

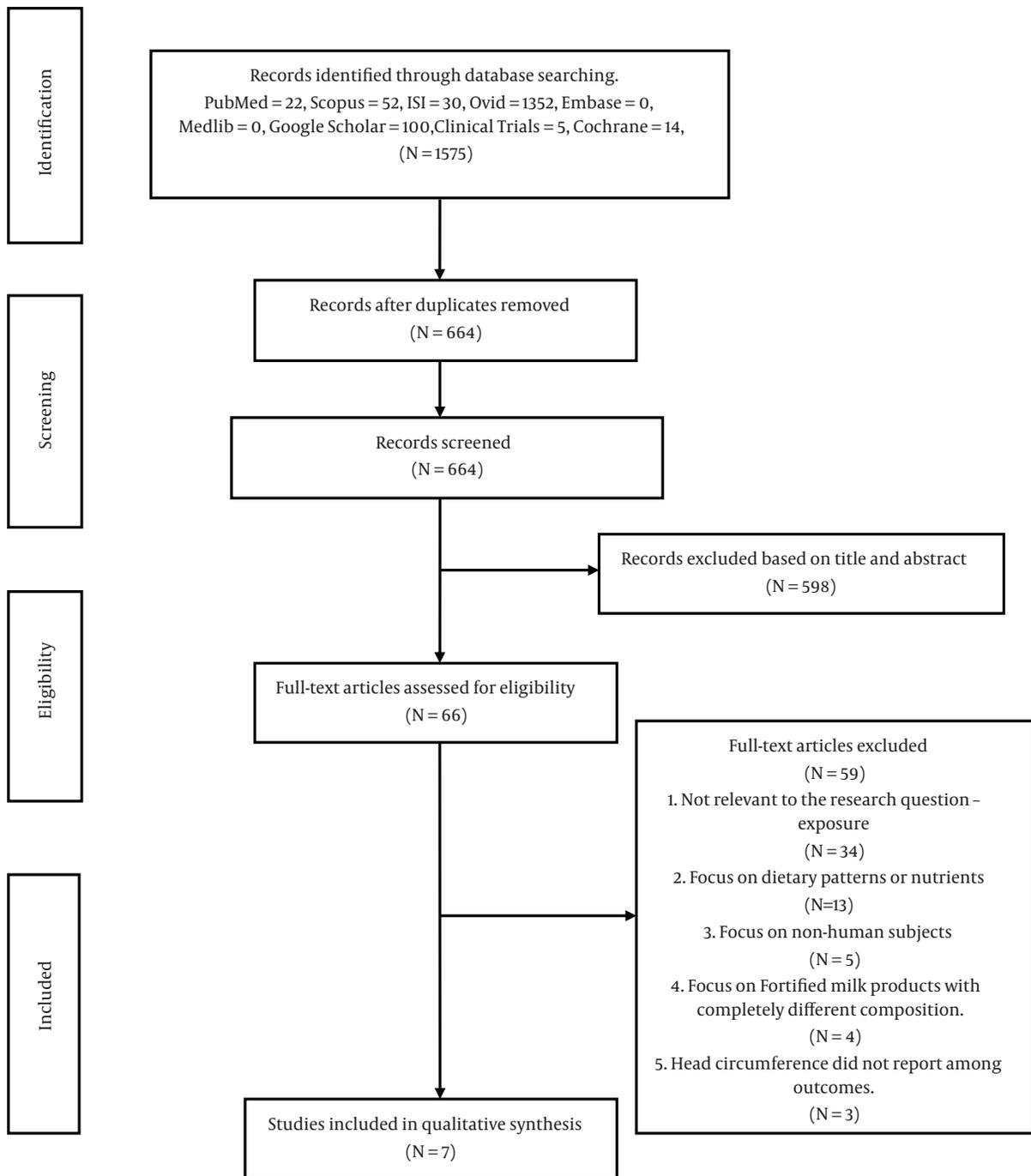


Figure 1. Flow Diagram of Study Selection

was suggestive of a positive relationship between milk or dairy products consumption during pregnancy and fetal head circumference.

### 7.1. Milk and Dairy Products and Neonatal Birth Head Circumference

Three prospective cohort studies that were conducted in Denmark, Netherlands and India with three different

sample sizes of 50117, 3405, and 797 respectively, indicated that maternal milk and dairy products intake had a positive effect on neonatal birth head circumference (15-17).

The specific strength of the cohort from Denmark was its large sample size. The Netherland cohort obtained detailed information on milk and dairy consumption, which was appropriate for a separate analysis. The Indian cohort used developed community-specific methods for estimating dietary intake, and they reported data about the consumption of various food groups as well as nutrient intakes. However, the other strengths of these studies were: using the prospective design, a validated food frequency questionnaire (FFQ), and collecting information about the extensive range of potential confounding factors.

The limitation of the Denmark cohort study was the use of last menstrual period (LMP) at  $\approx$  eight weeks or other non-precise information at  $\approx$  30 weeks instead of the exact method of ultrasound for the prediction of gestational age; this was an important confounding factor, which could cause in bias the results. The Netherland cohort had some limitations such as using the validated FFQ for older white female population; or assessing maternal milk consumption only once during pregnancy, thus they were unable to determine whether the associations were primarily due to milk consumption in the first trimester or later in pregnancy.

Three studies, one cohort study (12), one cross-sectional study (13) and one randomized controlled trial (14) showed that maternal milk or dairy products intake were not associated with neonatal birth head circumference.

In a small prospective cohort study on 279 Canadian females, who restricted their milk intake, low milk intake was not associated with birth head circumference (12). This study used cup, plate, bowl and ruler to assist estimating portion size of the interviewers and participants. However, the study had a small sample size. In a cross-sectional study in India (N = 156), the researchers didn't find any association between maternal milk consumption and neonatal birth head circumference (13). A randomized clinical trial showed no significant association between intakes of snack containing milk powder and birth head circumference. The strengths of this study were the random design, and the use of health workers from the community that maximized participant cooperation. The limitations included impossibility of full blindness or thought of getting a healthier snack, and these could have modified the behaviours and bias the results. Approximately 40% - 50% of women were fully compliant, and compliance was lower in the treatment group when compared to the control.

## 7.2. Milk and Dairy Products intake during pregnancy and Fetal Head Circumference

A cross-sectional study reported a positive relationship between maternal milk and dairy products consumption and fetal head circumference (13). Two cohort studies that were conducted in Netherlands, and in African-American adolescent population (age  $\leq$  17 years) of USA, showed no significant association between maternal milk, and dairy products consumption and fetal head circumference (16, 18).

Many factors in milk can promote fetal growth, but collinearity association among dietary constituents such as milk protein and dietary calcium makes it difficult to evaluate the role of single nutrients. Regarding the association of protein (dairy or non-dairy) with neonatal birth measures, the Danish cohort (15) suggested that the association could not be explained by the protein effect. In the Canadian cohort (12) no independent association of protein, calcium or riboflavin were observed with neonatal birth sizes in healthy mothers but it has been suggested that vitamin D contributes to the association between milk consumption and fetal growth. While according to the Dutch cohort (16), vitamin D is unlikely to contribute to this association because, in the Netherlands, milk is not fortified with vitamin D so milk consumption was not associated with higher intake of vitamin D.

Nowadays, cow's milk, because of modern methods for processing, has a high content of sex steroids especially estrogen, which has a known stimulating effect on fetal growth (21, 22). Another potential explanation can be related to the higher blood concentration of insulin growth factor I (IGF-I) after milk consumption; IGF-I is an important regulator of postnatal growth (23, 24). Some researchers have hypothesized that water-soluble substances in milk increase fetal growth; however they did not conclude that the growth-stimulating effect of cow's milk was clearly beneficial and more research is needed to identify causative factors and overall health implications (15). In total, the mechanism of the relationship of maternal milk and dairy products consumption with fetal and neonatal anthropometric measurements is unknown. However, hormones and micronutrients, rather than macronutrients and energy seem to be more likely involved in milk and dairy products.

As strength, we had no search limitations. The major limitation of the present review was the scarcity of eligible studies and substantial variability between them. However, other limitations include bias and residual confounding for dietary assessment, different methods of dietary assessment (Three studies used FFQ with different number of items, one used 24-hour recalls, and three studies used

both of them), and different range of milk or dairy products consumption.

## 8. Conclusions

According to the evidences in this systematic review, a positive association was concluded between maternal milk and dairy products consumption with neonatal birth head circumference in healthy females. However, the corresponding figure was not significant for fetal head circumference. It is noteworthy to mention that nearly all papers included in this review had highlighted the importance of milk and dairy products in the maternal diet as a source of protein, vitamin D, calcium, zinc, and other nutrients.

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**Table 1.** Description of Seven Included Studies Comprising of Four Prospective Cohorts, One Cross-Sectional and One Randomized Controlled Trial

Reference	Publication Year	Type of Study Country	No. of Participants Year of study	Age	Exposure	Outcomes	Confounder Adjustment	Quality
Heppe et al. (16)	2011	Prospective cohort; Netherlands	N = 3405; 2001 - 2005	Mean (SD); 31.4 (4.4)	Primary: Milk consumption (glasses/day) Secondary: Macronutrients from milk/dairy	Fetal head circumference, femur length and fetal weight were estimated by ultrasound, and birth weight, length and head circumference	A range of relevant maternal characteristics and other dietary intakes, including total energy	8 stars <sup>a</sup>
Mannion; et al. (12)	2006	Prospective cohort; Canada	N = 279; 1997 - 1999	19 - 45 year; mean age 31 y	Milk consumption ( $\leq$ 250 mL vs. $>$ 250 mL/day).	Infant birth weight, crown heel length and head circumference	Maternal characteristics included gestational weight gain. Other foods/nutrients were also considered	8 stars <sup>a</sup>
Olsen et al. (15)	2007	Prospective cohort; Denmark	N = 50,117; mother-infant pairs; 1996 - 2002	30.4 years in women reporting no milk consumption and 28.2 year in the high consumption group	Milk consumption by 8 categories (glasses/day) and protein from total dairy consumption (g/day)	Birth length and weight (Risk of SGA and LGA), abdominal circumference, placental weight and head circumference	Gestational age, infant's gender, maternal age, height, BMI, parity, gestational weight gain, smoking, energy intake, paternal height and family socioeconomic status	8 stars <sup>a</sup>
Chang et al. (18)	2003	Retrospective chart review within a prospective cohort of African American adolescents; USA	N = 350; 1990 - 2000	$\leq$ 17 years; Mean (SD); 15.9 (1.1)	Dairy intake, 5 categories, reduced into three levels of intake (high, medium, low) for further analysis.	Fetal femur length, birth weight, fetal biparietal diameter, fetal head circumference and fetal abdominal circumference	Gestational age, biparietal diameter, maternal age and height, pre-pregnancy BMI. Association with total energy and other nutrients was considered.	8 stars <sup>a</sup>
Rao et al. (17)	2001	Prospective cohort; India	N = 797; 1994 - 1996	15 - 40 year; mean age; 21.4 y	Milk products consumption by 4 categories (frequency)	Birth weight; crown heel length, triceps and subscapular skinfold thickness, head circumference, MUAC, abdominal circumference and placental weight.	Baby's gender, gestational age at delivery, maternal parity, pregnancy weight, energy intake, activity, social class, weight gain up to 28 weeks and fat intake.	8 stars <sup>a</sup>

Borazjani (13)	2010	Cross-sectional India	N = 156 2010	19 - 38 year; Mean (SD); 28.48(14.23)	Focus on different foods including dairy.	Head circumference, bipartietal diameter, abdomen circumference and femur length.	Maternal characteristics and other foods.	10 stars <sup>b</sup>
Potdar et al. (14)	2014	Non-blinded randomized controlled trial India	N = 6513 divided into two groups; 3205 in treatment group and 3308 in control groups. 2006 - 2012	< 40 year Median (IQR) 25 (22,28)	Treatment snacks contained green leafy vegetables, fruit and milk (snack/day).	Birth weight, rates of LBW, crown heel length, head circumference, midupper arm circumference, chest circumference, trips and subscapular skinfold thickness.	Gestational age, infant gender, age of newborn, maternal BMI, height, parity, age, socioeconomic status, gestational diabetes, education, compliance and baseline food intakes.	3 scores <sup>c</sup>

<sup>a</sup>Quality assessment according to the Newcastle-Ottawa scale (NOS).

<sup>b</sup>Quality assessment according to the adapted NOS.

<sup>c</sup>Quality assessment according to the Jadad quality assessment score.

**Table 2.** Description of the Dietary Assessment Methods, Time Period Covered, Exposure Quantity and Range and Results of the Studies

Reference	Study Design	Diet Method and Time of Assessment	Time Period Covered	Exposure and Average Intake	Range of Exposure	Results
Heppeet al. (16)	Prospective cohort	Modified version of a semi quantitative FFQ, at enrolment (median 13.5 weeks of gestation). Additional questions on milk and milk products.	Previous 3 months, covering intake within the first trimester.	Primary: Milk consumption (glasses/day) in 4 categories. Glass $\approx$ 150 mL. Median milk consumption was 2.6 glasses/day (interquartile range 2.1 glass/day)	0 - 1 glass/day; > 1 - 2 glasses/day; > 2 - 3 glasses/day; > 3 glasses/day	They found no consistent associations of maternal milk consumption with longitudinally measured fetal head circumference. Milk consumption of > 2 - 3 glasses/day was associated with a 2.2-cm (95% CI: 0.2 - 4.2) larger head circumference at birth (P = 0.03).
Mannion et al. (12)	Prospective cohort	Repeated 24 hours recalls (3 - 4 times) by trained interviewers using cups, plates, bowls and rulers for estimating quantity.	Habitual intake	Milk consumption by two categories. The study recruited females, who restricted their milk intake. Average milk consumption was not reported.	$\leq$ 250 mL/day ( $\leq$ 1 glass) > 250 mL/day (> 1 glass)	No influence of milk consumption on infant head circumference at birth.
Olsen et al. (15)	Prospective cohort	A 360-item FFQ was completed $\approx$ week 25 of gestation referring to the previous 4 weeks.	Previous 4 weeks, $\approx$ week 21 - 25 in pregnancy.	Primary: Milk consumption (glass $\approx$ 200 mL/day) and yoghurt (portion $\approx$ 150 mL/day) aggregated into glasses/day in 8 categories (cheese and ice-cream were excluded). Average milk consumption was $3.1 \pm 2.0$ glasses/day. Secondary: Protein from total dairy consumption (g/day)	0; > 0 - 1 glass/day; > 1 - 2 glasses/day; > 2 - 3 glasses/day; > 3 - 4 glasses/day; > 4 - 5 glasses/day; > 5 - 6 glasses/day; > 6 glasses/day	Mean infant head circumference showed increases across the whole range of milk intake (P < 0.001). After adjustment for confounding, the total increments were 0.13 cm (95% CI: 0.04 - 0.25 cm)
Chang et al. (18)	prospective cohort	24-hour dietary recall and FFQ administered by a registered dietician (RD) at first prenatal visit.	Habitual intake according to a combination of 24 hours recall and FFQ.	Dairy intake, servings/day, was divided to 5 categories, further reduced into high ( $\geq 3$ ), medium (2-3) and low (< 2) intake. No average consumption was reported, but 51% of women were in the low intake group (< 2 serving/day). One serving $\approx$ 1 glass $\approx$ 260 mL milk.	<1-0 serving/day <2-1 servings/day <3 servings/day <4-3 servings/day $\geq 4$ servings/day	No significant associations of dairy intake with fetal head circumference (P = 0.713) was present after correction for gestational age, maternal height, and pre-pregnancy BMI.

<b>Rao et al. (17)</b>	prospective cohort	24-hour recall was administered at 18 and 28 week of gestational by one of four nutritionists and a 111-item FFQ during the preceding 3-month period.	Previous 3 months and at 18 and 28 weak of gestation.	Milk products consumption (frequency) in 4 categories.	Never; < 1×/weeks; > 1×/weeks; ≥ Alternate days	The frequency of milk consumption at 18 weeks gestation was related to infant head circumference. This relationship was stronger at 18 weeks than at 28 weeks gestation (P < 0.01).
<b>Borazjani (13)</b>	Cross-sectional	Repeated 24 hours recalls (3 times) and FFQ.	Habitual dietary intake	Milk consumption (mL/day) in 5 categories. Cup ≈ 150 mL. Average milk consumption was 310.41 ± 154.76 mL/day.	None; < 150 mL/day; 150 - 300 mL/day; 300 - 450 mL/day; > 450 mL/day	There was a positive contribution between maternal milk intakes toward fetal head circumference. No association was found between milk intakes of the expectant mothers during pregnancy period with head circumference of baby.
<b>Potdar et al. (14)</b>	Nonblinded randomized controlled trial	A 91-item FFQ data collected at enrolment.	Over the preceding month	Treatment snacks contained green leafy vegetables, fruit and commercially bought full-fat milk powder (snack/day).	1 snack/day=1 ≥ 0/5 snack/day=0/5 < 0/5 snack/day=0	Findings showed no significant association between intakes of snack containing milk powder and birth head circumference