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ORIGINAL ARTICLE

The associations of high birth weight with blood pressure and hypertension in later life: a systematic review and meta-analysis

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The 'fetal origin hypothesis' suggests that metabolic diseases are directly related to poor nutritional status in early life. Thus, a high birth weight (HBW) may pose a lower risk than normal birth weight. Overweight and overnutrition are among the most widely recognized risk factors of metabolic diseases. To explore the possible effects of HBW on blood pressure and hypertension, a systematic review was performed. The PubMed and Embase databases were searched for relevant studies. The outcomes included systolic blood pressure (SBP), diastolic blood pressure (DBP) and hypertension. We included all of the studies that assessed the differences in outcomes for children aged >1 year between those born with normal birth weight (birth weight between 2500 and 4000 g or between the 10th and 90th percentiles for their gestational age) and those born with HBW (birth weight ⩾4000 g or ⩾90th percentile for their gestational age). The outcomes were analyzed descriptively and by conducting a meta-analysis. Thirty-one studies satisfied the inclusion criteria. The mean difference in blood pressure and the relative risk of hypertension between individuals with HBW and individuals with normal birth weight was inversely associated with age. SBP and DBP, as well as the prevalence of hypertension, were higher in younger children with HBW but lower in older adults with HBW compared with individuals with normal birth weight. The findings suggested that an individual with HBW is prone to hypertension and higher blood pressure during childhood. However, a 'catch-down' effect in the elevation of blood pressure is observed in subjects with HBW as they grow older. Thus, older individuals with HBW are less susceptible to hypertension than those with normal birth weight.
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Keywords: blood pressure; high birth weight; meta-analysis; systematic review

INTRODUCTION

Birth weight is an important indicator of the nutrition and growth status of fetuses. Poor nutrition in pregnancy often leads to low birth weight, whereas overnutrition leads to high birth weight (HBW).[1,2] Barker *et al.*[3] showed that reduced fetal growth increases cardiovascular disease mortality in adults. The 'fetal origin hypothesis' of adult diseases was introduced to explain the relationship between low birth weight and adult diseases.[4] Numerous studies on low birth weight have shown that birth weight is inversely related to the risk of metabolic syndrome,[5–8] which is defined as a combination of at least three of the following five components: obesity, high blood pressure, high serum triglycerides, low serum high-density lipoprotein and impaired glucose or insulin resistance.[9] The 'fetal origin hypothesis' also suggests that an adverse intrauterine environment (for example, characterized by poor nutrition) may reduce fetal growth by programming metabolic development and thus lead to lifelong physiological changes that predispose the body to metabolic diseases.[10]

HBW, which is also termed macrosomia or large for gestational age in obstetrics, is defined as birth weight >4000 g or >90th percentile of gestational age.[11] HBW is usually associated with maternal obesity, excessive gestational weight gain, or gestational diabetes mellitus.[12] As the prevalence of maternal obesity and gestational diabetes mellitus has increased worldwide, the prevalence of HBW has also increased.[13–14]

According to the 'fetal origin hypothesis', HBW may elicit effects on blood pressure that differ from those for individuals with low birth weight and normal birth weight (NBW; defined as birth weight between 2500 g and 4000 g); that is, subjects with HBW may have a lower risk of metabolic diseases than those with NBW. However, overnutrition and overweight in multiple stages of an individual's life are key risk factors for metabolic syndromes. Therefore, conflicting

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hypotheses have been proposed to explain the relationship between HBW and blood pressure. However, most published studies have focused primarily on low birth weight without considering subjects with HBW, or they have mixed subjects with HBW into the NBW group, making the comparison more heterogeneous.[7,15–18]

We performed this systematic review to clarify the relationship between HBW and blood pressure, to explain the paradox of the 'fetal origin hypothesis' for HBW, and to assess the effects of HBW on blood pressure and hypertension in later life compared with individuals of NBW.

METHODS

The systematic review and meta-analysis were conducted by following the Meta-Analysis of Observational Studies in Epidemiology Group checklist,[19] a checklist that includes the processes by which the data are obtained, the analysis is performed, and the findings are reported in meta-analyses.

We performed a literature search in the PubMed and Embase databases using the following terms: ('birth weight' OR 'birth size' OR 'macrosomia' OR 'large for gestational age') NOT ('preterm birth' OR 'low birth weight' OR 'small for gestational age' OR 'prematurity' OR 'twin') AND ('metabolic syndrome' OR 'hypertension' OR 'cardiovascular disease' OR 'blood pressure'). The search was limited to studies with human subjects that were published in the English language. The publication dates were before October 2012. Two authors screened the search results independently. The screened results from each reviewer were combined after deliberation. The full text articles were retrieved and checked for eligibility.

To be eligible for inclusion, studies had to satisfy the following criteria: (1) the study was an original report on the relationship(s) between birth weight and blood pressure or hypertension; (2) the subjects were singletons born at full-term; (3) the outcomes were investigated at ages >1 year; (4) HBW and NBW were distinctly defined with HBW as $\geqslant 4000$ g or $\geqslant$ the 90th percentile for gestational age and NBW as 2500–4000 g or the 10–90th percentiles for gestational age.

Furthermore, a manual search was conducted among the reference lists for all of the eligible studies and related reviews. The overall process is illustrated in Figure 1.

From the studies that were considered eligible for this review, two authors collected information independently using standardized sheets. The means and the s.d. values for blood pressure were determined directly or by performing calculations. The numbers of participants with hypertension in each group were obtained for the relative risk (RR) calculations. If possible, all of the original data were extracted using the minimum subgroups.

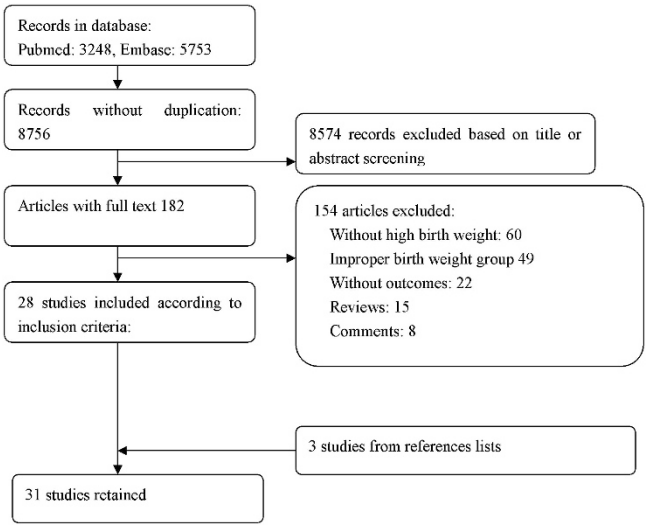

Figure 1 Flow chart of literature review.

The Newcastle-Ottawa quality assessment scale was used for quality assessment.[20] Eight factors were assessed, and each satisfactory factor received one star (a maximum of nine stars were used).

We used STATA version 11.0 (Stata Corp., College Station, TX, USA) for the data analysis. The heterogeneity among the studies was assessed using Q and I^2.[21] The data were synthesized using a random-effects model or a fixed-effect model according to the heterogeneity. Meta-regression was used to confirm the heterogeneity and the relationship between the characteristics of the studies and the effects of HBW.

RESULTS

Overall

We obtained 8756 records of studies from the PubMed and Embase databases in the computer search. After the abstracts of the studies were screened, 182 potentially relevant studies remained. We further assessed the details, performed a manual search, and determined that 31 studies satisfied the inclusion criteria. We primarily excluded studies because they lacked an HBW group. We also excluded those with inappropriate birth weight groups (that is, the cutoff points for HBW and NBW did not satisfy the inclusion criteria).

Blood pressure and/or hypertension data were obtained from 31 studies, and some of them were included in this review. In particular, six studies provided mean values but no standard deviations; another study provided Z scores. These seven studies were not included in the meta-analysis.

Four studies focused on overweight or obesity. Furthermore, at least one study included the following types of participants: offspring with gestational diabetes mellitus, children with abnormal urinalysis, individuals with type 1 diabetes and women with pregnancy-induced hypertension. The characteristics of the 31 studies are summarized in Table 1.

The quality of the studies in terms of subject selection, as well as the comparability and reliability of outcomes, is summarized in Table 2.

Systolic blood pressure

Fourteen studies provided 24 mean differences (MDs) in SBP between individuals with HBW and NBW. The meta-analysis of random effects revealed an overall MD of –0.25 mm Hg (95% confidence interval, –0.92, 0.42) with considerable heterogeneity ($I^2 = 79.3\%$, Q-statistic: $P < 0.0001$). The subgroup analysis by age (using the mean age from each study) showed that only the age group >40 years exhibited low heterogeneity. As the individuals grew older, the MD in SBP changed from positive to negative. The results indicate that HBW is associated with higher SBP in younger subjects, but lower SBP in older subjects (Figure 2).

To explore the sources of heterogeneity in the pooled MD, we performed a meta-regression analysis, which revealed that age explains the majority of the variance between the studies (value of adjusted R^2). The regression coefficient also indicates that age was inversely associated with the MD in SBP (Table 3).

Among the seven studies excluded from the meta-analysis, all five studies on adults showed that SBP was lower among individuals with HBW than individuals with NBW (statistical test unavailable).[45–49] One of the two studies on children showed that SBP was higher among those with HBW than those with NBW (non-significant),[23] in agreement with the results shown in Figure 2.

Diastolic blood pressure

Thirteen studies provided 23 MDs in DBP between those with HBW and those with NBW. The pooled MD was 0.20 mm Hg (95%

Table 1 Brief descriptions of the studies including in this review

Reference, country, year born	*Study design*	*Characters of subjects*	*Source of BW and sex*	*Define of HBW/NBW*	*Mean age (years) of outcomes (range)*	*Subgroup*	*No. of HBW/ No. of NBW*	*Outcome (HBW compared with NBW)*
Chiavaroli*et al.*[22] Italy 1997–2004	CS	Clinic patients; White; First born; Prepubertal; Healthy mother	R M,F	>90th PGA/10th ~90th PGA	6 (4–9) 7 (4–9)	NW Obese	16/15 16/15	Mean of SBP: HBW>NBW, SI Mean of DBP: HBW>NBW, NS Mean of SBP: HBW>NBW, SI Mean of DBP: HBW>NBW, NS
Evagelidou *et al.*[23],[a] Greece NA	CS	Caucasian; Prepubertal; Healthy mother	R M,F	>95th PGA/10th ~90th PGA	6 (6–7)	NA	31/33	*Z*-score Mean of SBP:HBW>NBW, NS *Z*-score Mean of DBP:HBW>NBW, NS
Boney *et al.*[24] USA NA	CH	Offspring of GDM and matched by Non-GDM	R M,F	>90th PGA/10th ~90th PGA	6,7,9,11	OGDM ONGDM	42/52 43/42	All RR of hypertension:<1 NS All RR of hypertension:<1 NS
Hirschler *et al.*[25] Argentina 1994–2002	CS	Public school children	R M,F	>4000 g/ 2500~4000 g	9 (5–13)	NA	95/860	Mean of SBP: HBW>NBW, NS
Bouhours-Nouet *et al.*[26] France 1986–1998	CS	Simple obesity in Clinic; Healthy mother	R M,F	>90th PGA/10th ~90th PGA	11 (6–15)	NA	32/52	Mean of SBP: HBW<NBW, NS Mean of DBP: HBW<NBW, NS
Eyzaguirre *et al.*[27] Chile NA	CS	Simple obesity in Clinic; Higher socioeconomic status	R M,F	>90th PGA/10th ~90th PGA	10 (2–18)	NA	132/763	Mean of SBP: HBW=NBW, NS Mean of DBP: HBW>NBW, NS RR of hypertension:>1 NS
Wang *et al.*[28] China NA	CS	Overweight attended hospital; No siblings	R M,F	>90th PGA/10th ~90th PGA	10 (NA)	NA	60/312	RR of hypertension:>1 SI
Guerrero-romero *et al.*[29] Mexico NA	CS	School children; No ethnic mixture; No smoking	Q M,F	Mean:4041 g/ Mean:3272 g	11 (7–15)	NA	97/1088	Mean of SBP: HBW<NBW, NS Mean of DBP: HBW<NBW, NS RR of hypertension:>1 SI
Wei *et al.*[30] Taiwan 1974–1991	CS	School children with abnormal urinalysis	R M,F	>4000 g/2500–4000 g	11 (6–18)	Boy Girl	2510/26508 2497/45111	Mean of SBP: HBW<NBW, SI Mean of DBP: HBW<NBW, SI RR of hypertension:>1 SI Mean of SBP: HBW<NBW, SI Mean of DBP: HBW<NBW, SI RR of hypertension:>1 SI
Seidman *et al.*[31] Israel 1964–1971	CH	Born in 1964–1971 with military medical records	R M,F	>4000 g/2500–4000 g	17 (NA)	Man Women	1859/17764 628/11445	Mean of SBP: HBW=NBW, NS Mean of DBP: HBW=NBW, NS Mean of SBP: HBW<NBW, NS Mean of DBP: HBW>NBW, SI
Renom *et al.*[32] Brazil 1978–1979	CC	LGA from a birth cohort	R M,F	>90th PGA/10~90th PGA	24 (23–25)	NA	117/398	Mean of SBP: HBW>NBW, SI Mean of DBP: HBW>NBW, SI

Table 1 (Continued)

Reference, country, year born	*Study design*	*Characters of subjects*	*Source of BW and sex*	*Define of HBW/NBW*	*Mean age (years) of outcomes (range)*	*Subgroup*	*No. of HBW/ No. of NBW*	*Outcome (HBW compared with NBW)*
Euser *et al.*[33] Norway 1967–1977	CS	Aged over 20 in one county; Caucasian; no pregnancy	R M,F	>90th PGA/10th ~90th PGA	24 (20–30)	NA	749/5999	Mean of SBP: HBW>NBW, NS Mean of DBP: HBW<NBW, NS RR of hypertension: =1 NS
Järvelin *et al.*[34] Finland 1966	CH	Born and lived in Finland; White	R M,F	>4000 g/ 2500 ~4000 g	31 (NA)	Men Women	579/2179 374/2627	Mean of SBP: HBW<NBW, SI Mean of DBP: HBW<NBW, NS Mean of SBP: HBW<NBW, NS Mean of DBP: HBW>NBW, NS
Fagerudd *et al.*[35] Finland NA	CS	Type 1 diabetes from health institutions; Diabetes onset<36 year of age	R M,F	>90th PGA/10th ~90th PGA	33 (NA)	NA	155/1234	Mean of SBP: HBW<NBW, SI Mean of DBP: HBW<NBW, NS RR of hypertension: <1 NS
Hardy *et al.*[36] UK 1946	CH	Born and still lived in Britain	R M,F	>4000 g/ 2500–4000 g	36 (NA) 43 (NA) 53 (NA)	M F M F M F	217/1340 113/1414 205/1318 107/1357 193/1189 96/1278	Mean of SBP: HBW<NBW, NS Mean of DBP: HBW>NBW, NS Mean of SBP: HBW>NBW, NS Mean of DBP: HBW>NBW, NS Mean of SBP: HBW<NBW, SI Mean of DBP: HBW>NBW, NS Mean of SBP: HBW<NBW, NS Mean of DBP: HBW<NBW, NS Mean of SBP: HBW<NBW, SI Mean of DBP: HBW<NBW, SI Mean of SBP: HBW<NBW, NS Mean of DBP: HBW<NBW, NS
Liew *et al.*[37] US 1923–1944	CH	Adults from four US communities	Q/R M,F	4000–4500 g/ 2500–4000 g	59 (55–74)	Black and white White	1095/8282 932/6686	Mean of SBP: HBW<NBW, SI Mean of DBP: HBW<NBW, SI RR of hypertension: <1 SI Mean of SBP: HBW<NBW, SI Mean of DBP: HBW<NBW, NS RR of hypertension: <1 SI
Curhan *et al.*[38] USA 1911–1946	CH	Healthy Professionals in US	Q M	>4504 g/ 2497 ~4494 g	52 (40–75) 61 (48–83)	NA	1745/19974 1745/19974	RR of hypertension: >1 NS RR of hypertension: <1 SI
Curhan *et al.*[39] USA 1911–1946	CH	Registered nurses in US	Q M	>4504 g/ 2497 ~4494 g	35 (25–42) 40 (30–55) 55 (45–60)	NA	1178/84334 1676/61620 1676/61620	RR of hypertension: >1 SI RR of hypertension: <1 NS RR of hypertension: >1 NS
Eriksson *et al.*[40] Finland 1924–1933	CH	Born and Still live in Finland	R M,F	>4000 g/ 2500 ~4000 g	67 (62–72)	Men Women	446/3048 248/2080	RR of hypertension: <1 NS RR of hypertension: <1 NS
Eriksson *et al.*[41] Sweden 1913	CH	Born and lived in Gothenburg	R M	>4250 g/ 3000 ~4250 g	80 (NA)	NA	91/311	RR of hypertension: <1 SI

Table 1 (Continued)

Reference, country, year born	*Study design*	*Characters of subjects*	*Source of BW and sex*	*Define of HBW/NBW*	*Mean age (years) of outcomes (range)*	*Subgroup*	*No. of HBW/ No. of NBW*	*Outcome (HBW compared with NBW)*
Rich-Edwards *et al.*[42] USA 1921–1946	CH	Registered nurses; Free from CHD and stroke	Q F	>4536 g/ 2495–4536 g	44 (30–55)	NA	1638/60110	RR of hypertension:<1 NS
Innes *et al.*[43] USA 1970∼	CC	PIH in the first pregnancy matched with non-PIH	R F	>4000 g/ 2500∼4000 g	21 (12–28)	NA	1624/21643	RR of PIH:>1 SI
Li *et al.*[44,a] USA NA	CS	Child lived in Birmingham; Prepubertal; Healthy	R M,F	>4000 g/ 2500–4000 g	8 (8∼14)	NA	18/61	Mean of SBP:HBW<NBW, NT
Leon *et al.*[45,a] Sweden 1973–1976	CH	Born in 1920–1924 with military medical records	R M	>4000 g/ 2750–4000 g	18 (NA)	NA	33449/ 124024	Mean of SBP:HBW<NBW, NT
Clausen *et al.*[46,a] Denmark 1961–1974	CH	Born and live in Copenhagen; Non-pregnancy; Caucasians	R M,F	>4000 g/ 2500–4000 g	25 (18–32)	Men Women	16/40 19/133	Mean of SBP:HBW<NBW, NT Mean of SBP:HBW<NBW, NT
Leon *et al.*[47,a] Sweden 1920–1924	CH	Born and lived in Uppsala in 1970–1973	R M	>4250 g/ 3250–4250 g	49 (48–51)	NA	119/908	Mean of SBP:HBW<NBW, NT Mean of DBP:HBW<NBW, NT
Fall *et al.*[48,a] UK 1923–1930	CH	Born and still lived in Hertfordshire	R F	>4309 g/ 2948–4309 g	64 (60–71)	NA	12/217	Mean of SBP:HBW<NBW, NT
Yliharsila *et al.*[49,a] Finland 1924–1933	CH	Born and still live in Finland; Normotension	R M,F	>4000 g/ 2500–4000 g	70 (65–75)	NA	21/255	Mean of SBP:HBW<NBW, NT
Bowers *et al.*[50] China 1998–2002	CH	Termborn kids form Kindergartens	R M,F	>4000 g/ 2500–4000 g	4 (3–6)	NA	1977/13708	RR of hypertension:<1 NS
Koupilova *et al.*[51] Sweden 1920–1924	CH	Born and lived in Uppsala in 1970–1973	R M	>4250 g/3250∼ 4250 g	50,60,70	50 Y 60 Y 70 Y	120/908 62/455 62/455	RR of hypertension:<1 NS RR of hypertension:<1 SI RR of hypertension:<1 SI
Sørensen *et al.*[52] Denmark 1941–1961	CS	People living in one town of Denmark	R M	>4000/3300–4000 g	41 (30–50)	NA	72/127	Mean of SBP:HBW>NBW, NS Mean of DBP:HBW<NBW, NS

Abbreviations: BW, birth weight; CC, case–control; CH, cohort; CS, cross-section; DBP, diastolic blood pressure; F, female; HBW, high birth weight; LGA, large for gestational age; M, male; NA, not available; NBW, normal birth weight; NS, no significant; NT, no test; OGDM, offspring of gestational diabetes mellitus; ONGDM, offspring of non-gestational diabetes mellitus; PGA, percentile of gestational age; PIH, pregnancy-induced hypertension; Q, questionnaire; R, record; RR, risk ratio; SBP, systolic blood pressure; SI, significant.
[a]Not included in meta-analysis.

Table 2 Assessment of quality of the study

		Selection				*Comparability*		*Outcome*			
Study	*Design*	☆	☆	☆	☆	☆	☆	☆	☆	☆	*Total score*
Chiavaroli *et al.*[22]	CS		☆	☆	☆	☆		☆	☆	☆	7
Evagelidou *et al.*[23,a]	CS		☆	☆	☆	☆		☆	☆	☆	7
Boney *et al.*[24]	CH		☆	☆	☆	☆		☆	☆		6
Hirschler *et al.*[25]	CS	☆	☆	☆	☆			☆	☆	☆	7
Bouhours-Nouet *et al.*[26]	CS		☆	☆	☆			☆	☆	☆	6
Eyzaguirre *et al.*[27]	CS		☆	☆	☆			☆	☆	☆	6
Wang *et al.*[28]	CS		☆	☆	☆			☆	☆	☆	6
Guerrero-romero *et al.*[29]	CS	☆	☆		☆			☆	☆	☆	6
Wei *et al.*[30]	CS		☆	☆	☆	☆		☆	☆	☆	7
Seidman *et al.*[31]	CH	☆	☆	☆	☆	☆	☆	☆	☆	☆	9
Renom *et al.*[32]	CC	☆	☆	☆	☆	☆		☆	☆	☆	8
Euser *et al.*[33]	CS	☆	☆	☆	☆	☆		☆	☆		7
Järvelin *et al.*[34]	CH	☆	☆	☆	☆	☆	☆	☆	☆	☆	9
Fagerudd *et al.*[35]	CS		☆	☆	☆				☆	☆	5
Hardy *et al.*[36]	CH	☆	☆	☆	☆	☆	☆	☆	☆	☆	9
Liew *et al.*[37]	CH	☆	☆		☆			☆	☆		5
Curhan *et al.*[38,39]	CH		☆		☆		☆		☆		4
Eriksson *et al.*[40]	CH	☆	☆	☆	☆	☆		☆	☆		7
Eriksson *et al.*[41]	CH	☆	☆	☆	☆	☆	☆	☆	☆		8
Rich-Edwards *et al.*[42]	CS		☆		☆		☆		☆		4
Innes *et al.*[43]	CC	☆	☆	☆	☆	☆		☆	☆		7
Li *et al.*[44,a]	CS	☆	☆	☆	☆			☆	☆		6
Leon *et al.*[45,a]	CH	☆	☆	☆	☆	☆	☆	☆	☆	☆	9
Clausen *et al.*[46,a]	CH		☆	☆	☆		☆	☆	☆		7
Leon *et al.*[47,a]	CH	☆	☆	☆	☆	☆	☆	☆	☆		8
Fall *et al.*[48,a]	CH	☆	☆	☆	☆		☆	☆	☆		7
Yliharsila *et al.*[49,a]	CH	☆	☆	☆	☆	☆		☆	☆		7
Browser *et al.*[50]	CH	☆	☆	☆	☆	☆		☆	☆	☆	8
Koupilova *et al.*[51]	CH	☆	☆	☆	☆	☆	☆	☆	☆		8
Sørensen *et al.*[52]	CS		☆	☆	☆	☆		☆	☆	☆	7

Abbreviations: CC, case–control; CH, cohort; CS, cross-section.
[a]Not included in meta-analysis.

confidence interval, –0.23, 0.62). The heterogeneity among these studies was also high ($I^2 = 72.6\%$, Q-statistic: $P < 0.0001$). A subgroup analysis by age showed that the heterogeneity in each group was low. With increasing age, the MD in DBP changed from positive to negative. The results indicate that HBW is associated with higher DBP in younger subjects but lower DBP in older subjects (Figure 3).

The same characteristics of the subjects and the studies mentioned above were included in the meta-regression. The results of the meta-regression showed that age might be the main factor contributing to the significant heterogeneity. The regression coefficient also showed that age was inversely associated with the MD in DBP (Table 4).

Of the two studies that were excluded from the meta-analysis, one study reported that adults with HBW had lower DBP than those with NBW (statistical test unavailable).[47] The other study revealed that DBP was higher in children with HBW than those with NBW (not a statistically significant difference)[23] (Figure 3).

Hypertension

Fifteen studies with 31 RRs for hypertension associated with HBW and NBW were included. The overall RR combination was 1.00 (95% confidence interval, 0.931, 1.06) with significant heterogeneity ($I^2 = 63.8\%$, Q-statistic: $P < 0.0001$). The subgroup analysis showed that there was heterogeneity in the age group >40 years. With increasing age, the RR for hypertension changed from >1 to <1. The results indicate that HBW is associated with a higher risk of hypertension in younger subjects but a lower risk in older subjects (Figure 4).

The sources of heterogeneity were investigated by performing meta-regression analysis. The results of the meta-regression show that age was the primary, statistically significant source of heterogeneity (Table 5). Age was inversely associated with the RR of hypertension, indicating that older subjects with HBW had a lower risk of hypertension than those with NBW (Figure 4).

DISCUSSION

In this review, we primarily aimed to assess the effects of HBW on blood pressure and hypertension by summarizing the current evidence from published studies. However, substantial heterogeneity made it inappropriate to synthesize all of the data. In particular, the subgroup analysis showed that some subgroups exhibited high heterogeneity. Further meta-regression analysis revealed that age was consistently associated with the effects of HBW on blood pressure and the risk of hypertension.

The results of both the meta-combination and meta-regression analysis revealed that age was inversely associated with the effects of HBW on blood pressure and hypertension. The results indicate that HBW has contrasting effects on blood pressure and hypertension in

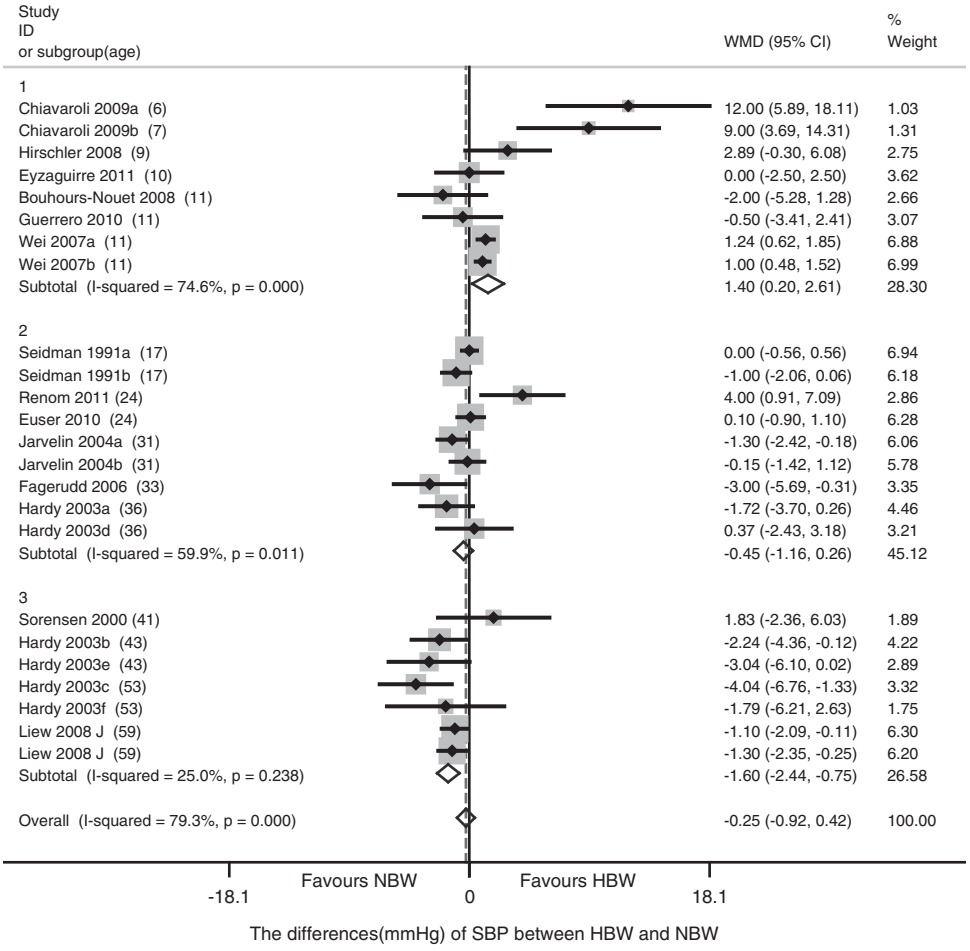

Figure 2 The differences of systolic blood pressure (SBP) between HBW and NBW in meta-analysis. Studies ordered by mean ages at which the outcome was measured. The pooled MDs were calculated by means of a random effects model; 95% confidence intervals (CI) are shown in parentheses and as horizontal bars. HBW, high birth weight, NBW, normal birth weight, WMD, weighted mean difference.

Table 3. Meta-regression for the MD of SBP between HBW and NBW

Predictor	*Coefficient*	*s.e.*	*t*	P	*95% CI*	*Adj.* R-*squared*
Characters of subjects						
Age	−0.065	0.023	−2.86	0.009	−0.112, −0.018	67.68%
Gender 1	1.562	1.088	1.44	0.165	−0.694, 3.819	−18.86%
Gender 2	−1.339	1.188	−1.13	0.272	−3.803, 1.124	−11.67%
Healthy status	0.871	1.260	0.69	0.497	−1.741, 3.483	1.11%
Characters of studies						
% HBW	13.553	4.680	2.90	0.008	3.848, 23.258	−3.75%
Study quality	−0.218	0.367	−0.59	0.559	−0.979, 0.543	−15.55%
Sample size	0.000	0. 000	0.58	0.570	−0.000, 0.000	2.45%
Publication year	0.111	0.097	1.14	0.266	−0.090, 0.312	−11.54%
Study design	1.744	0.963	1.81	0.084	−0.254, 3.742	41.65%

Abbreviations: MD, mean difference, SBP, systolic blood pressure; HBW, high birth weight, NBW, normal birth weight.
Gender 1: $M+F=1$, $F=0$; Gender 2: $M=1$, $F=0$; Healthy status: from ordinary population = 0, from clinic population = 1; proportion of HBW: number of HBW/(number of HBW + number of NBW); study quality: NOS score; sample size: number of HBW + number of NBW; study design: cohort = 0, cross-section and case–control = 1 Regression method: ReML (residual maximum likelihood); Regression model: univariate regression with random-effects.

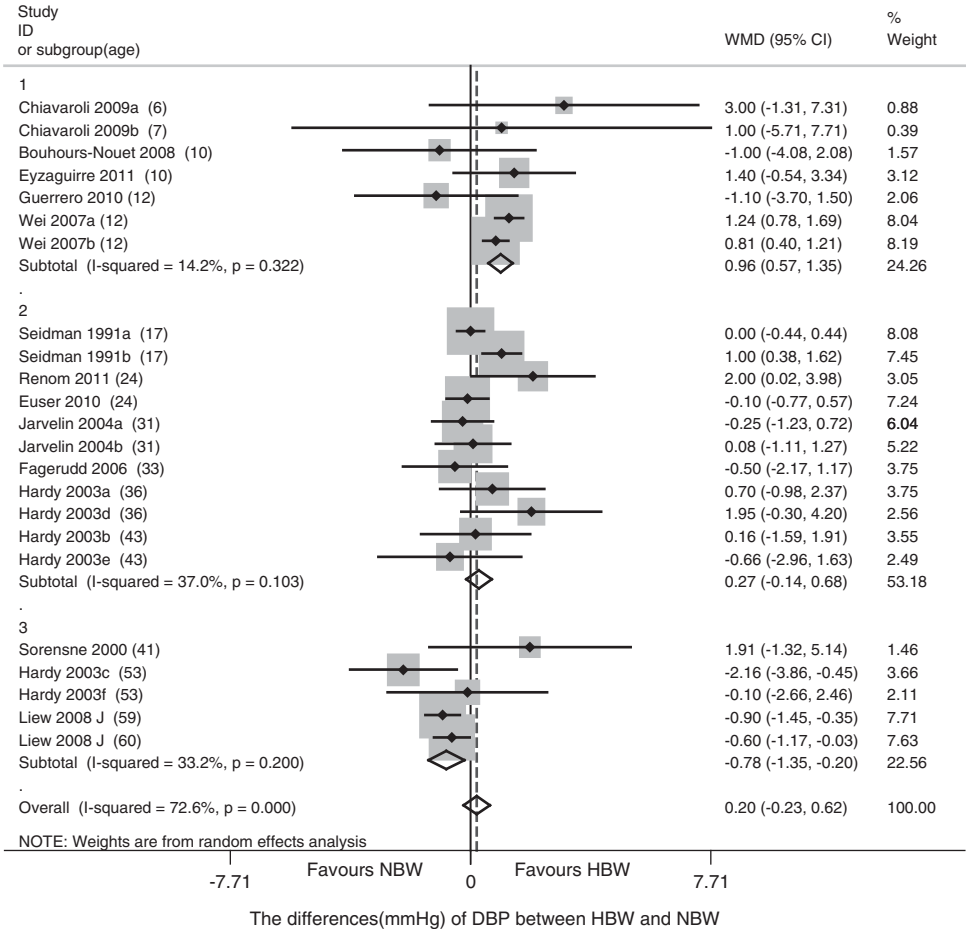

Figure 3 The differences of diastolic blood pressure (DBP) between HBW and NBW in meta-analysis. Studies ordered by the mean age at which the outcome was measured. The pooled MDs were calculated by means of a random-effects model; 95% confidence intervals (CI) are shown in parentheses and as horizontal bars. HBW, high birth weight; NBW, normal birth weight, WMD, weighted MD.

Table 4 Meta-regression for the MD of DBP between HBW and NBW

Predictor	*Coefficient*	*s.e.*	*t*	P	*95% CI*	*Adj. R-squared*
Characters of subjects						
Age	−0.034	0.008	−4.42	0.000	−0.050, −0.018	77.92%
Gender 1	−0.581	0.414	−1.40	0.175	−1.442, 0.280	27.04%
Gender 2	−0.019	0.465	−0.04	0.968	−0.986, 0.949	−10.45%
Healthy status	0.911	0.409	2.22	0.037	−0.059, 1.763	39.54%
Characters of studies						
% HBW	1.144	2.868	0.40	0.694	−4.820, 7.108	−10.36%
Study quality	0.136	0.135	1.01	0.323	−0.144, 0.417	5.30%
Sample size	0.000	0.000	1.42	0.169	−0.000, 0.000	19.10%
Publication year	−0.011	0.036	−0.31	0.759	−0.086, 0.064	−9.55%
Study design	0.491	0.430	1.14	0.266	−0.403, 1.386	13.16%

Abbreviations: CI, confidence interval; DBP, diastolic blood pressure; HBW, high birth weight, MD, mean difference; NBW, normal birth weight.
Gender 1: $M+F=1$, $F=0$; Gender 2: $M=1$, $F=0$; healthy status: from ordinary population = 0, from clinic population = 1; proportion of HBW: number of HBW/(number of HBW + number of NBW); study quality: NOS score; sample size: number of HBW + number of NBW; study design: cohort = 0, cross-section and case–control = 1 Regression method: ReML (residual maximum likelihood); Regression model: univariate regression with random-effects.

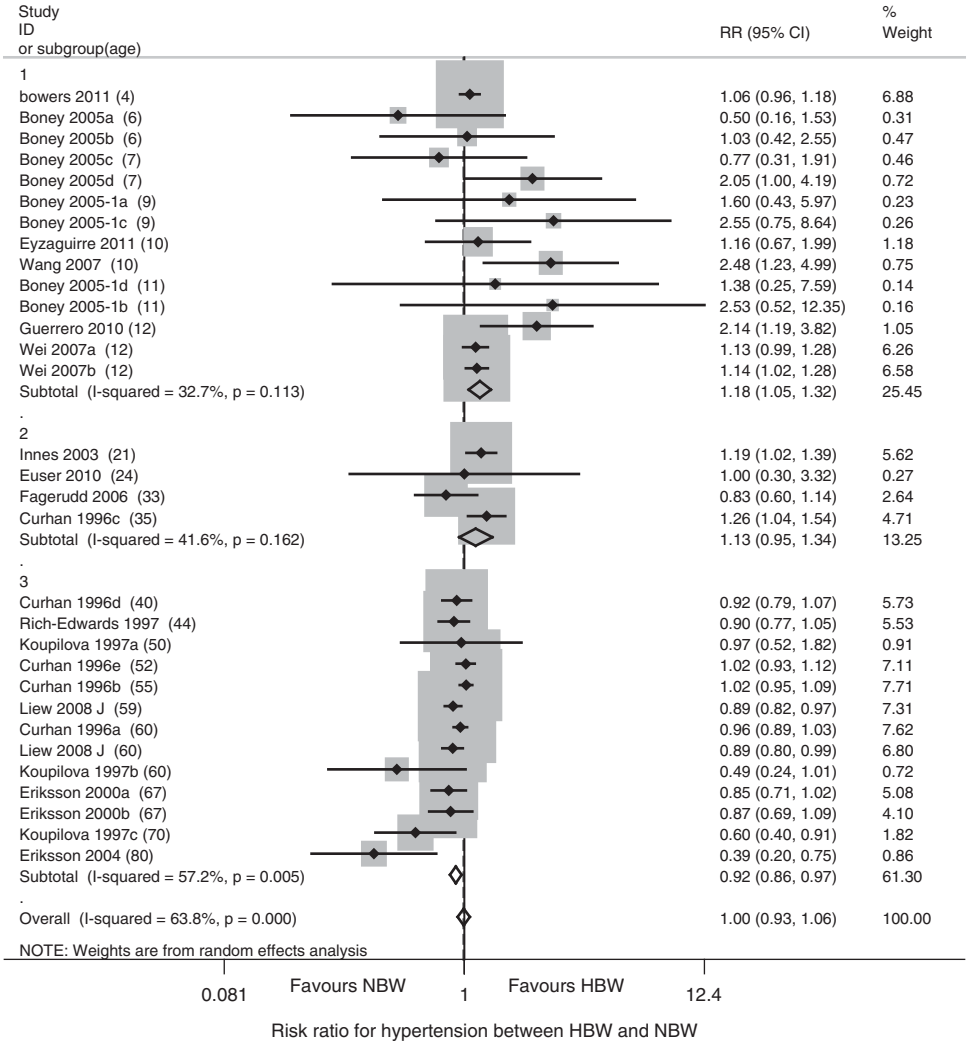

Figure 4 Risk ratio for hypertension between HBW and NBW in meta-analysis. Studies ordered by the mean age at which the event was checked. The pooled risk ratios were calculated by means of a random-effects model; 95% confidence intervals (CI) are shown in parentheses and as horizontal bars. HBW, high birth weight, NBW, normal birth weight, RR, risk ratio.

Table 5 Meta-regression for the RR of hypertension between HBW and NBW

Predictor	*Coefficient*	*s.e.*	*t*	P	*95% CI*	*Adj.* R-*squared*
Characters of subjects						
Age	−0.006	0.002	−3.58	0.001	−0.009, −0.003	79.59%
Gender 1	0.259	0.135	1.92	0.064	−0.016, 0.535	−60.23%
Gender 2	−0.276	0.148	−1.87	0.072	−0.578, 0.026	−23.71%
Healthy status	0.138	0.152	0.90	0.373	−0.174, 0.449	11.85%
Characters of studies						
% HBW	−0.511	0.577	0.89	0.383	−0.668, 1.690	−40.07%
Study quality	−0.011	0.048	−0.24	0.813	−0.109, 0.086	−55.70%
Sample size	0.000	0.000	0.01	0.995	−0.000, 0.000	−43.89%
Publication year	0.018	0.012	1.47	0.153	−0.007, 0.044	−48.52%
Study design	0.194	0.121	1.60	0.121	−0.054, 0.442	31.16%

Abbreviations: CI, confidence interval; HBW, high birth weight, NBW, normal birth weight; RR, relative risk.
Gender 1: $M+F=1$, $F=0$; Gender 2: $M=1$, $F=0$; Healthy status: from ordinary population = 0, from clinic population = 1; proportion of HBW: number of HBW/(number of HBW + number of NBW); study quality: NOS score; sample size: number of HBW + number of NBW; study design: cohort = 0, cross-section and case–control = 1 Regression method: ReML (residual maximum likelihood); Regression model: univariate regression with random-effects.

younger subjects compared with older subjects. In the younger subjects, HBW resulted in higher blood pressure and a higher risk of hypertension than NBW. In older subjects, HBW led to lower blood pressure and a lower risk of hypertension.

HBW, which indicates overnutrition in the initial stage of life, raised blood pressure and the risk of hypertension in early life. Another published systematic review also reported that newborns with higher birth weight had higher blood pressure.[16] Although an age-related increase in blood pressure has been observed in almost every population,[53] the increase in blood pressure associated with HBW seems to be attenuated or reversed with increasing age. In other words, a 'catch-down' effect occurs in blood pressure and the risk of hypertension when individuals with HBW grow older.

In fact, a 'catch-down' phenomenon is common in babies born large. For example, large for gestational age babies usually experience a postnatal 'catch-down' in height, weight and so on.[54,55] The increase in blood pressure likely follows the same pattern for weight or height in large babies, with this increase subsiding after several years.

Evidence has shown that subjects with HBW are usually bigger in size and heavier in weight.[56] However, these subjects are more metabolically healthy when they grow older because they have more lean mass than adipose tissue.[57] This condition may lead to lower blood pressure in subjects with HBW compared with those who have the same BMI but were born with NBW. Another possible explanation is that the difference in blood pressure between those with HBW and NBW is very subtle in childhood, and other factors compensate for these differences later in life.

To the best of our knowledge, this review is the first to discuss the association of HBW with blood pressure and hypertension over the life course. This review reveals that age is an important factor that is associated with birth weight and affects blood pressure and hypertension. Considering the conflicting implications of HBW (that is, an overweight status in the early stage of life does not correspond to a high risk of hypertension in later stages of life), we propose that the 'catch-down' effect in blood pressure might attenuate the risk of hypertension associated with HBW.

However, this review has some limitations. First, only studies published in English were eligible for the study, which may have introduced selection bias. Second, given that age is the main source of heterogeneity, subgroup meta-analyses of more specific age groups may be more effective when additional evidence is available. Third, subjects with HBW are a heterogeneous population that includes both individuals from diabetic pregnancies or obese mothers and normal large infants with birth weights that align with their growth potential. Considering that information on the etiology of fetal overgrowth is not reported in most studies, the effects of specific causes of HBW on blood pressure remain unclear.

CONCLUSION

The MDs in blood pressure and in the RR of hypertension between individuals with HBW and NBW are inversely associated with age. Blood pressure and the risk of hypertension are higher among individuals with HBW during childhood but lower during adulthood. This finding may be partially attributed to the 'catch-down' effect in the elevation of blood pressure when the subjects with HBW grow older.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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