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REVIEW

Prognostic factors for cesarean section outcome of pregnant women with gestational diabetes mellitus: a systematic review and meta-analysis

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Objective: To evaluate the prognostic factors for cesarean section outcome of pregnant women with diabetes mellitus.

Methods: MEDLINE, EMBASE, Cochrane Library, CBM, CNKI and Wanfang database were searched. Two researchers independently screened the literature, extracted data, and evaluated the risk of bias of included studies. For pooled data with factors of perioperative outcome, the RevMan software was used for data translation and meta-analysis. The result is shown intuitively with the bubble diagram of evidence mapping by Excel 2016.

Results: We included 12 randomized controlled trials (RCTs) in the meta-analysis. Twelve RCTs with 1,390 patients were included in the systematic review. The results show that the perioperative blood glucose management regimens, preoperative fasting and water deprivation, anesthesia regimens, postoperative fluid regimens, postoperative analgesia regimens, postoperative wound care regimens, psychological interventions, different dosing regimens for antibiotics, and obesity may affect the cesarean section outcome of diabetic mothers and newborns. The evidence for all the outcomes was low quality.

Conclusion: Many prognostic factors have shown significant association with postoperative outcomes of cesarean section. More clinical research evidence with high-quality is needed.

Keywords: gestational diabetes mellitus, caesarean section, prognostic factors, systematic review, meta-analysis, evidence mapping

Background

In pregnant women with gestational diabetes mellitus (GDM), the overall cesarean section rate was accounted for 35.3%.[1] Simultaneously, compared with nondiabetic pregnant women, diabetic maternal acute cesarean section rate was reported 1.52 times of GDM.[2] Diabetes is an important risk factor for surgical incision infection,[3] and for cesarean section, diabetes is an important risk factor for maternal postoperative wound infection as well.[4] Thus, the pregnancy with diabetes and the management of special risk factors are important, and the existing systematic evaluation shows that effective treatment and control of GDM can reduce preeclampsia, shoulder dystocia, and the incidence of huge children.[5] In addition, several systematic reviews have concentrated on the effects of certain specificc factors based on the health outcomes of pregnant women with GDM, such as the effects of different glycemic management regimens on glycemic control and maternal and child outcomes,[6–10] and effects of dietary intervention or nutritional

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therapy based on maternal and child outcomes.[11,12] For patients with cesarean section with GDM, there have been several studies evaluating differences in patients' outcomes under different conditions, such as anesthesia,[13–15] postoperative fluid regimen,[16,17] and postoperative wound care.[18] However, there is no systematic review regarding the current evaluation of the factors affecting the maternal and child's outcomes during the period of affecting by GDM. This study was designed to assess the risk factors associated with perioperative outcomes in pregnant women with GDM.

Methods

Inclusion and exclusion criteria

Inclusion criteria: 1) pregnant women suffered cesarean section with GDM; 2) exposure factors for cesarean outcomes; 3) RCTs; and 4) reported perioperative outcomes, such as blood glucose level, Apgar scores, adverse effects, and so on. Exclusion criteria: 1) there were no specific outcome data to assess the impact of exposure factors on patients with perioperative outcomes; 2) non-English and Chinese published research, 3) summary of unpublished meeting.

Literature search

We conducted a systematic search on Medline (via PubMed), EMBASE, Cochrane Library, CBM, CNKI and Wanfang, using the terms Diabetes, Gestational, Diabet*, "Cesarean Section", caesarean, "diabetes, pregnancy", "gestational diabetes mellitus", "cesarean section", "cesarean section", "caesarean section". The retrieval date was February 28, 2018.

Study screening

Two researchers independently screened the literature titles, abstracts, and the full text. A pre-test was performed prior to formal screening of the literature to ensure that each researcher truly perceived the screening criteria and process. Discrepancies between the two reviewers were resolved by consensus discussion.

Data extraction

The two researchers independently extracted the following data from the pre-designed information extraction table: year of publication, name of journal, the first author's affiliation, place and duration of study, funding, conflict of interest, type of study, sample size, basic characteristics of study object, exposure factors, and associated outcome data. A pretest was conducted before formal extraction to ensure that each researcher agrees with the extraction criteria and process. If there are some differences, they could be solved through discussion.

Risk of bias assessment

Two researchers used the Cochrane risk of bias tool was used for bias risk assessment of randomized controlled trials. A pretest was conducted before the formal evaluation to ensure that each researcher agrees with the evaluation criteria and process. In case of existence of some differences, they could be solved by a third researcher.

Data consolidation and analysis

In the RevMan 5.3 software, the RR and 95% CI were used to combine the binary data, and the data were merged using the mean difference (MD) and 95% CI. The data combination uses a random-effect model. The heterogeneity was included in the study by Cochran's Q test ($P<0.05$ denotes heterogeneity) and I^2 test. When the number of inclusion indicators is ≥10, the publication bias is evaluated by making a funnel plot; conversely, the qualitative analysis was included in the study funding, the conflict of interest, and the outcome to discuss the possibility of publication bias.

Quality of evidence

The quality of the evidence was graded according to the principles of the GRADE approach used in the evaluation of prognostic studies[19,20] and in a previous study (as example).[21] (These factors may lead to rating down the quality of evidence in GRADE system) and the three upgraded factors (large effect, dose-response, and plausible confounders) to determine the final level of evidence. Quality of evidence was ranked as high, medium, low, and very low-level using the results of summary table.

Evidence mapping

Excel 2016 was used to integrate the RR value from meta-analysis and GRADE. The result is shown intuitively with the bubble diagram. Due to heterogeneity of MD for the outcome, we did not make a bubble diagram for MD value from meta-analysis.

Results

Study selection

There are 13,447 articles identified by literature search. After duplicates were removed in endnote, 11,585 records titles and abstractswere reviewed, 142 articles were retrieved full-text reviewing. Finally, a total of 12 randomized controlled trials[14,16–18,22–29] involving 1,390 patients were included for meta-analysis (Figure 1).

Characteristics of the included studies

The studies were published in 2010 and 2017, the sample sizes ranged from 33 to 201. All studies were from China. The participant age was from 24 to 39. The two studies[16,23] were funded by nonprofit funds, one study reported that there was not the conflict of interest, and the rest of the study did not report funding (Table 1).

Risk of bias for included studies

The included RCTs were only low risk of bias in incomplete outcome data and selective reporting (Figure 2); 8 studies[14,17,18,24–26,29] did not report random sequences; 1 study[27] reported that there was a high risk of bias in random sequences; none of the studies reported allocation concealment; 6 studies[16,18,26–29] did not blind the researchers and patients, and they likely contained an impact on the results; 8 studies[14,18,22–26,29] did not blind the outcome evaluators, and they likely contained an influence on the results.

Prognostic factors

Insulin pump

One randomized controlled study[25] reported a total of 3 outcomes. It was revealed that duration of treatment process (MD=−5.30, 95% CI: −5.78~−4.82, $P<0.00001$), insulin dosage (MD=17.00, 95% CI: −23.04~−10.96, $P<0.00001$), and the incision healing duration (MD=−4.40, 95% CI: −5.58~−3.22, $P<0.00001$) of the repeated subcutaneous injection for insulin group were superior to those of the insulin pump group, and the difference was statistically significant (Appendix 1).

Short-term fasting and water deprivation

One randomized controlled study[27] reported a total of 11 outcomes. Preoperative blood glucose concentrations

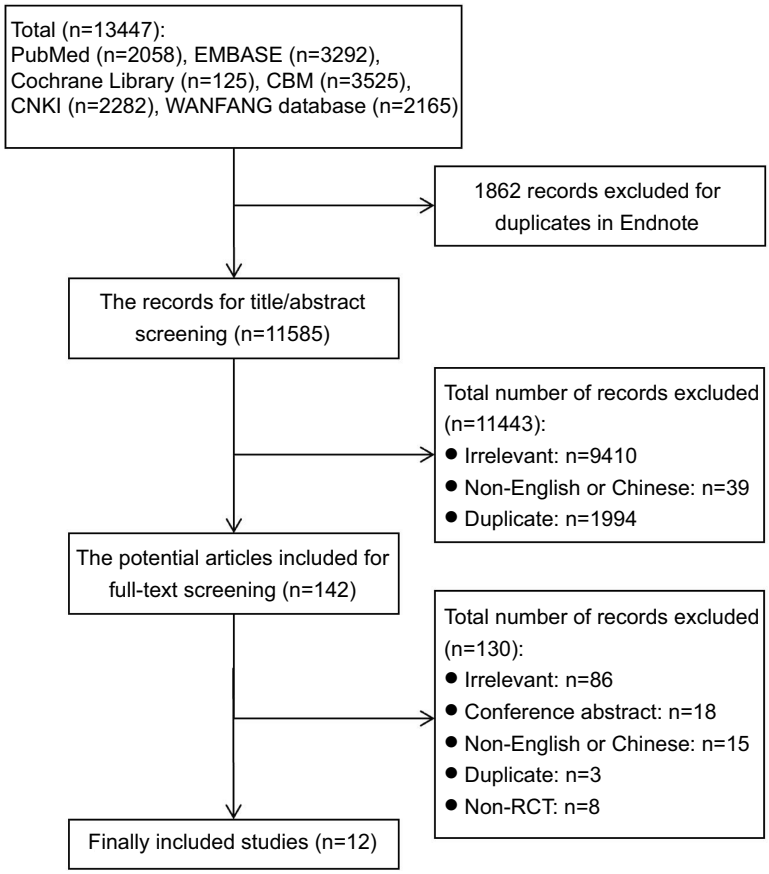

Figure 1 The screening flow chart.

Table 1 Basic characteristics of included studies

	Year	Country	Funding	Conflict of interest	Time of research	Sample size	Prognostic factors	Exposed group (Mean±SD)			Nonexposed group (Mean ±SD)		
								Age	Weight (kg)	Gestation (weeks)	Age	Weight (kg)	Gestation (weeks)
Li 2010[25]	2010	China	○	○	2007.1~2009.12	48	Insulin pump	Range: 24~36	○	○	Range: 24~36	○	○
Feng 2017[27]	2017	China	○	○	2015.4~2015.9	162	Short-term fasting and water-deprivation	32.91 ±4.00	○	38.74±1.54	4.07 ±4.39	○	38.28±1.47
Wang 2017[28]	2017	China	○	○	2014.1~2016.2	110	Individual health education	○	○	○	○	○	○
Wang 2010[16]	2010	China	●[a]	○	2009.2~2010.3	70	Fructose Injection	○	○	○	○	○	○
Zhao 2011[24]	2011	China	○	○	2011.3~2011.7	33	PCEA	29.7 ±3.7	76.7±6.3	○	30.1 ±4.1	77.2±6.2	○
Yu 2014[17]	2014	China	○	○	2011.5~2013.10	201	Fructose Injection	31.8 ±6.9	○	38.8±1.9	31.8 ±6.9	○	38.8±1.9
Chen 2015[18]	2015	China	○	○	2012.9~2013.9	140	Microwave treatment for post-operative wound	26.4 ±2.9	○	○	26.4 ±2.9	○	○
Han 2015[22]	2015	China	○	○	2012.2~2014.1	153	Psychological intervention	25.13 ±5.24	○	26.05±0.23	25.13 ±5.24	○	26.05±0.23
Li 2015[23]	2015	China	●[b]	○	2014.1~2015.5	200	Psychological intervention	30.05 ±2.51	○	○	29.03 ±1.56	○	○
Yin 2015[14]	2015	China	○	○	2014.3~2015.3	54	Epidural anesthesia	28.1 ±5.4	○	37.9±5.1	29.0 ±5.4	○	38.5±5.4
Zhang 2015[26]	2015	China	○	○	2012.3~2013.12	99	Low dose sufentanil combined with bupivacaine VS bupivacaine	30.7 ±2.1	78.2±8.1	37.8±1.0	30.2 ±2.0	77.7±7.3	38.1±0.9
Yang 2017[29]	2017	China	○	○	2016.2~2017.6	120	Addition of once antibiotic	27.2 ±3.25	○	○	29.1 ±4.03	○	○

Notes: ○: Unreported; ●: reported; [a]Liaoning Natural Science Foundation Project (20042089), Liaoning Education Department Fund Project (20062013); [b]Science and Technology Research and Development Plan of Hebei province(132777208).
Abbreviation: PCEA, patient-controlled epidural analgesia.

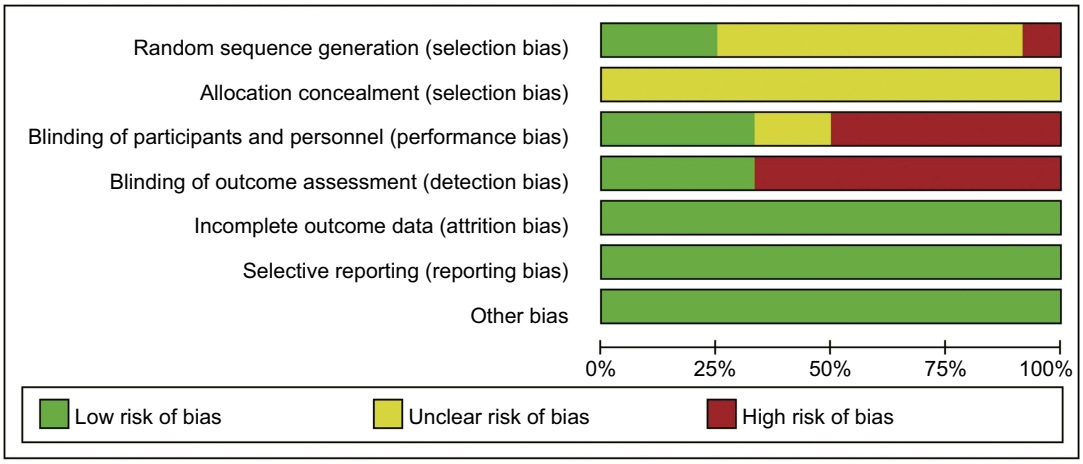

Figure 2 Risk of bias graph.

(MD=0.84, 95% CI: 0.42~1.26, *P*=0.001) and the level of blood glucose in newborn infants after birth (MD=0.45, 95% CI: −0.03~0.87, *P*=0.038) for short-term group were superior to those of long-term group, and the difference was statistically significant. Bleeding volume during cesarean section (MD=−42.71, 95% CI:−82.55~−2.86, *P*=0.039) for short-term group was inferior to long-term group, and the difference was statistically significant. There were no significant differences in postoperative blood sugar concentrations, the rates of nausea and vomiting, incidence of hypoglycemia in newborn infants after birth and mothers before cesarean section, duration of anus exhausting of puerpera, Apgar score 1 and 5 mins after delivery (Appendix 1).

Individual health education

A randomized controlled study[28] reported a total of 4 outcomes. Control rates for 2 hr plasma glucose (PG) (RR=1.31, 95% CI: 1.04~1.66, *P*<0.05) and midnight blood glucose (RR=1.23, 95% CI: 1.01~1.50, *P*<0.05) and the satisfaction rate of nursing services (MD=6.51, 95% CI: 5.80~7.22, *P*<0.01) for individualized health education group were superior to those of conventional health education group, and the difference was statistically significant. There were no significant differences in control rates of fasting blood glucose (FBG) as well (Appendix 1).

Fructose injection

Two randomized controlled trials[16,17] reported a total of 8 outcomes. The blood glucose levels 1.5–2 hours after infusion (MD=−1.17, 95% CI: −1.93~−0.41, *P*=0.003), blood glucose levels 3–4 hours after infusion (MD=−0.99, 95% CI: −1.61−0.36, *P*=0.002), the level of insulin 1.5 hours after infusion (MD=−13.50, 95% CI: −19.02~−7.98) (*P*<0.00001), and the level of insulin 3 hours after infusion (MD=−8.59, 95% CI: −13.75~−3.43, *P*=0.001) for fructose injection were superior to glucose and Insulin injection. The difference was statistically significant. There were no significant differences in blood glucose level, blood glucose level, urinary carcass positive rate, and urine sugar positive rate after transfusion, and no significant difference was found between the two groups (Appendix 1).

Patient-controlled epidural analgesia (PCEA)

A randomized controlled trial[24] reported a total of 13 outcomes. The level of blood glucose in presence of analgesia after 6 hours (MD=−0.80, 95% CI: −1.01 to −0.59, *P*<0.00001), 12 hours (MD=−0.76, 95% CI: −1.00 to −0.52, *P*<0.00001), 24 hours (MD=−0.65, 95% CI: −0.87 to −0.43, *P*<0.00001), and 36 hours (MD=−0.75,95% CI: −0.96~−0.54, *P*<0.00001) for the patient-controlled intravenous analgesia (PCIA) group was superior to PCIA group. The difference was statistically significant. There was no significant difference between the two groups (Appendix 1).

Microwave treatment for postoperative wound

A randomized controlled trial[18] reported a outcome (RR=1.15, 95% CI: 1.03~1.29, *P*=0.01, see Appendix 1, in which the difference was statistically significant (*P*<0.01) (Appendix 1).

Psychological intervention (including music therapy)

Two randomized controlled trials[22,23] reported a total of 14 outcome indicators, in addition to entering the operating room immediately with heart rate (MD=−0.86, 95% CI: −2.69~0.97, *P*=0.36), entering the operating room immediately with anxiety score (MD=−0.13, 95%

CI: −2.57~2.31, P=0.92), and the normal feeding rate (RR=1.07, 95% CI: 0.99–1.16, P=0.09). The difference between the two groups was not statistically significant. The rest of the outcome indicators for the psychological intervention group were inferior to the conventional nursing group, and the difference between the two groups was statistically significant (Appendix 1).

Epidural anesthesia

A randomized controlled trial[14] reported a total of six outcomes: glucose concentration at the of cutting skin (MD=1.48, 95% CI: 1.31~1.65, P<0.00001, 2 hours after delivery (MD=0.90, 95% CI: 0.71 to 1.09, P<0.00001) and 6 hours after delivery (MD=1.11, 95% CI: 0.93 to 1.29, P<0.00001), the epidural group were higher than the general anesthesia group, and the difference was statistically significant. The differences in the other outcomes between the two groups were not statistically significant (Appendix 1).

Low-dose sufentanil combined with bupivacaine of spinal-epidural anesthesia

One randomized controlled study[26] reported a total of 11 outcomes. Based on the report, glucose concentration at the time of cutting skin (MD=−1.45, 95% CI: −1.61~−129, P<0.00001), the blood glucose concentration 2 hours after delivery (MD=−0.89, 95% CI: −1.07~−071, P<0.00001), and the mean arterial pressure 5 mins after anesthesia (MD=5.80, 95% CI: 3.12~8.48, P<0.00001) were assessed. The difference was statistically significant. However, the differences for the other outcome indicators between the two groups were not statistically significant (Appendix 1).

Addition of once antibiotic

One randomized controlled study[29] reported a total of 12 outcomes. The treatment efficiency (RR=0.68, 95% CI: 0.04~1.66, P<0.05) of the addition of an antibiotic once group was inferior to 24 hours antibiotic application group, and the difference was statistically significant. There were no significant differences in response rate, overall response rate, the inefficiency rate, the duration of WBC <12×10^9/L, body temperature (without fever or returned to normal status 2 hours after surgery), and the grades A, B, and C of healing (Appendix 1).

Publication bias

The number of studies included in every outcome was <10; thus, it was unattempted to use funnel plot to assess the publication bias. All studies have not reported conflict of interest, and only 2 studies reported that the funding originated from the nonprofit grants.

Quality of evidence

The levels of evidence for all the outcome all is low on the GRADE system (see Appendix 2). The reasons for downgrading includes the risk of bias (no randomized sequence generation and allocation concealment, no blindness to researchers, patients and outcome evaluators) and inaccuracy (sample size is less than the optimal sample size and the confidence interval of the combined results cross invalid line).

Evidence mapping

Each bubble corresponds to one outcome for the prognostic factors. The size, color, and position of the bubbles were used to indicate the current research status. The size of the bubbles indicates the sample size, and the color of the bubbles indicates the quality of the evidence. The horizontal coordinate indicates the prognostic factors, the vertical coordinate indicates the RR of meta-analysis (Figure 3).

Discussion

The International Federation of Gynecology and Obstetrics (FIGO) guideline recommended to receive cesarean section to prevent shoulder dystocia or birth injury, when fetal weight would be>4,000 g.[30] For pregnant women with cesarean section, in addition to the conventional perinatal management, the integration of perioperative management is required, including blood sugar control, anesthesia, healthcare, etc. This study is the first systematic review of the prognostic factors. The results of the systematic review show that the perioperative blood glucose management regimens, preoperative fasting and water-deprivation regimens, anesthesia regimens, postoperative regimens, postoperative analgesia regimens, postoperative wound care regimens, psychological interventions, and different dosing regimens for antibiotics may affect the health outcomes of diabetic maternal and newborns. However, the quality of evidence was low, and more high-quality clinical research evidence is required.

According to the principle of GRADE method in the evaluation of a prognosis research system,[10,11] the quality of evidence for each outcome is low, and the reason of downgrading is mainly bias risk and inaccuracy. The bias risks included in the randomized controlled trials were assessed by the Cochrane Bias Risk Assessment Tool, in

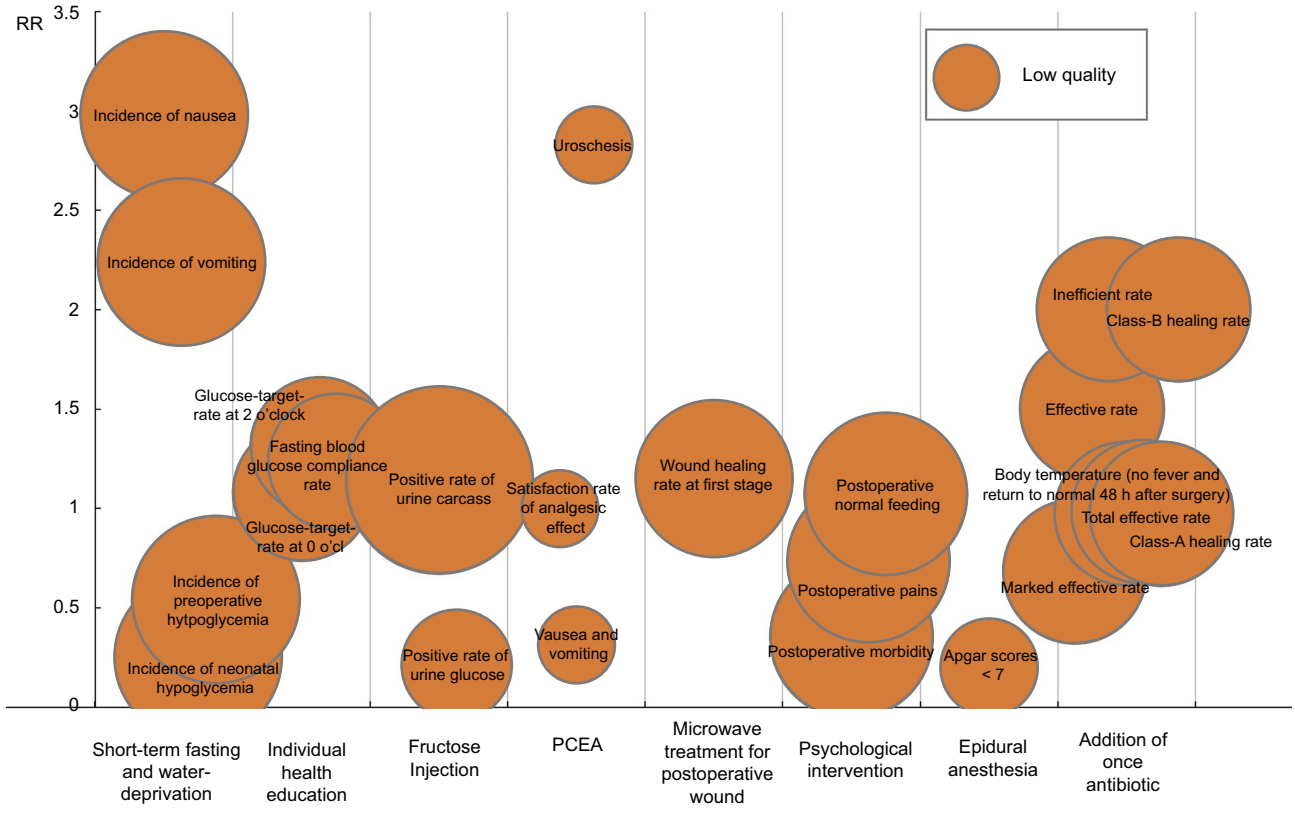

Figure 3 Summary of risk ratio and quality of evidence of outcomes for the prognostic factors with the bubble diagram.
Abbreviation: PCEA, patient-controlled epidural analgesia.

which the main source of bias was the nonreported random sequence generation and allocation concealment, which did not blind the researchers, the patients, and the outcome evaluators, and did not report the source of the information and the method of recruiting or joining the patients. The reason for the imprecision is that the sample size is less than the optimal sample size, and the CI of the effect sizes spans the invalid line. For publication bias, as the number of included studies was <10, the publication bias was not evaluated using a funnel plot. In addition, the included studies did not report the conflict of interest, considering the research topics and manufacturers that may be the interests of the relationship, and in addition to psychological intervention and obesity factors, the rest of the comparison groups were assessed by the possibility of publication bias. However, it was not possible to quantify the possibility of publication bias; thus, the publication bias was not considered in this study. In addition, because most of outcomes included only 1 study, a few outcomes included only 2 studies, and I^2 values are small, it is not been downgraded due to heterogeneity. We performed meta-analyses by using the random effects model for multiple risk factors and outcomes. The qualities of the evidence for all outcomes were low. As the number of studies increases and the quality of the research improves, new research data may change the results of this system review. Therefore, it needs to more new high-quality research to update the review in the future.

The main advantages of this systematic review are: 1) for the first time on the impact of pregnancy in patients with diabetes maternal–perinatal outcome of the perioperative factors were evaluated; 2) the original research carried out a systematic, comprehensive search, greatly reducing the possibility of missing; 3) the quality of evidence was graded by GRADE method, and the factors affecting the outcome of perioperative period of cesarean section in pregnant women with diabetes mellitus were clearly presented and interpreted. The limitations of the system review: 1) Only the studies published in Chinese and English were searched, the other languages were not be considered; 2) All the studies are from China, the results may not been applied to other countries and regions.

Conclusion

Low-quality evidence shows that perioperative blood glucose management regimens, anesthesia regimens, postoperative fluid regimens, postoperative analgesia regimens, postoperative wound care, and psychological interventions may affect the health outcomes of diabetic maternal and newborns.

Details of ethics approval

No ethics approval was required or sought for this review.

Data sharing statement

This review does not involve any analysis of individual patient data.

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Disclosure

The authors report no conflicts of interest in this work.

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Supplementary materials

Appendix 1. Effect evaluation results

Outcome	No. of studies	No. of participants	Effect estimate RR/MD (95%CI)	*P* value
Insulin pump VS multiple subcutaneous injections of insulin				
Blood glucose standard time (d)	1	48	**MD: -5.30 (-5.78, -4.82)**	<0.00001
Dose of insulin (U/d)	1	48	**MD: -17.00 (-23.04, -10.96)**	<0.00001
Surgical incision healing time /d	1	48	**MD: -4.40 (-5.58, -3.22)**	<0.00001
Fasting and water-deprivation: short-term VS long-term				
Preoperative blood glucose (mmol/L)	1	162	**MD: 0.84 (0.42, 1.26)**	0.001
Postoperative blood glucose(mmol/L)	1	162	MD: 0.16 (-0.17, 0.49)	0.345
Incidence of nausea	1	162	RR: 2.98 (0.77, 11.51)	0.180
Incidence of vomiting	1	162	RR: 2.24 (0.38, 13.03)	0.647
Incidence of neonatal hypoglycemia	1	162	RR: 0.25 (0.03, 2.02)	0.302
Incidence of preoperative hypoglycemia	1	162	RR: 0.54 (0.18, 1.63)	0.264
Maternal anal discharge time(h)	1	162	MD: -0.04 (-0.25, 0.17)	0.692
Bleeding during childbirth (ml)	1	162	**MD: -42.71 (-82.55, -2.86)**	0.039
Neonatal Apgar scores at 1 min	1	162	MD: 0.03 (-0.18, 0.24)	0.918
Neonatal Apgar scores at 5 min	1	162	MD: -0.03 (-0.14, 0.08)	0.183
Postnatal blood glucose (mmol/L)	1	162	**MD: 0.45 (0.03, 0.87)**	0.038
Health education: individualization VS convention				
Fasting blood glucose compliance rate	1	110	RR: 1.08 (0.86, 1.35)	>0.05
Glucose-target-rate at 2 o'clock	1	110	**RR: 1.31 (1.04, 1.66)**	<0.05
Glucose-target-rate at 0 o'cl	1	110	**RR: 1.23 (1.01, 1.50)**	<0.05
Nursing service satisfaction	1	110	**MD: 6.51 (5.80, 7.22)**	<0.01
Fructose Injection VS Glucose Injection + Insulin				
Blood glucose level at 1.5~2h after infusion (mmol/L)	2	202	**MD: -1.17 (-1.93, -0.41)**	0.003
Blood glucose level at 3~4h after infusion (mmol/L)	2	202	**MD: -0.99 (-1.61, -0.36)**	0.002
Blood glucose level at 6h after infusion (mmol/L)	1	70	MD: -0.62 (-1.86, 0.61)	0.32
Insulin level at 1.5h after infusion (mU/L)	1	132	**MD: -13.50 (-19.02, -7.98)**	<0.00001
Insulin level at 3h after infusion (mU/L)	1	132	**MD: -8.59 (-13.75, -3.43)**	0.001
Blood uric acid level at 3h after infusion (μmol/L)	1	132	MD: -8.00 (-34.96, 18.96)	0.56
Positive rate of urine carcass	2	202	RR: 1.14 (0.49, 2.64)	0.77
Positive rate of urine glucose	1	70	RR: 0.21 (0.01, 4.25)	0.31
PCEA VS PCIA				
Blood glucose level at 3h after the onset of analgesia (mmol/L)	1	33	MD: 0.01 (-0.21, 0.23)	0.93
Blood glucose level at 3h after the onset of analgesia (mmol/L)	1	33	**MD: -0.80 (-1.01, -0.59)**	<0.00001
Blood glucose level at 12h after the onset of analgesia (mmol/L)	1	33	**MD: -0.76 (-1.00, -0.52)**	<0.00001
Blood glucose level at 24h after the onset of analgesia (mmol/L)	1	33	**MD: -0.65 (-0.87, -0.43)**	<0.00001
Blood glucose level at 36h after the onset of analgesia (mmol/L)	1	33	**MD: -0.75 (-0.96, -0.54)**	<0.00001
VAS score at 36h after the onset of analgesia (mmol/L)	1	33	MD: -0.04 (-0.31, 0.23)	0.77
VAS score at 6h after the onset of analgesia (mmol/L)	1	33	MD: -0.01 (-0.20, 0.18)	0.92
VAS score at 12h after the onset of analgesia (mmol/L)	1	33	MD: -0.02 (-0.24, 0.20)	0.86
VAS score at 24h after the onset of analgesia (mmol/L)	1	33	MD: -0.05 (-0.39, 0.29)	0.77
VAS score at 36h after the onset of analgesia (mmol/L)	1	33	MD: -0.04 (-0.35, 0.27)	0.80

(*Continued*)

Appendix 1. (Continued).

Outcome	No. of studies	No. of participants	Effect estimate RR/MD (95%CI)	*P* value
Satisfaction rate of analgesic effect	1	33	RR: 1.00 (0.89, 1.12)	1.00
Vausea and vomiting	1	33	RR: 0.31 (0.01, 7.21)	0.47
Uroschesis	1	33	RR: 2.83 (0.12, 64.89)	0.51
Postoperative wound care: microwave treatment of VS routine care				
Wound healing rate at first stage	1	140	RR: 1.15 (1.03, 1.29)	0.01
Psychological intervention (including music therapy) VS routine care				
Systolic pressure immediately into the operating room (mmHg)	1	200	**MD: -9.80 (-12.42, -7.18)**	<0.00001
Systolic pressure after surgery into the operating room 30min (mmHg)	1	200	**MD: -35.37 (-38.32, -32.42)**	<0.00001
Intraoperative systolic pressure (mmHg)	1	153	**MD: -22.63 (-27.24, -18.02)**	<0.00001
Diastolic pressure immediately into the operating room (mmHg)	1	200	**MD: -3.58 (-5.20, -1.96)**	<0.00001
Diastolic pressure after surgery into the operating room 30min (mmHg)	1	200	**MD: -7.58 (-9.62, -5.54)**	<0.00001
Intraoperative diastolic pressure (mmHg)	1	153	**MD: -10.61 (-14.65, -6.57)**	<0.00001
Heart rate immediately into the operating room	1	200	MD: -0.86 (-2.69, 0.97)	0.36
Heart rate after surgery into the operating room 30min	1	200	**MD: -8.89 (-10.52, -7.26)**	<0.00001
Anxiety score immediately into the operating room	1	200	MD: -0.13 (-2.57, 2.31)	0.92
Anxiety score after surgery into the operating room 30min	1	200	**MD: -2.22 (-3.55, -0.89)**	0.001
Intro-operative hemorrhage (ml)	1	153	**MD: -62.39 (-78.31, -46.47)**	<0.00001
Postoperative morbidity	1	153	**RR: 0.35 (0.19, 0.64)**	0.0008
Postoperative pains	1	153	**RR: 0.73 (0.60, 0.89)**	0.002
Postoperative normal feeding	1	153	RR: 1.07 (0.99, 1.16)	0.09
Epidural anesthesia vs general anesthesia				
Blood glucose while skin cutting (mmol/L)	1	54	**MD: 1.48 (1.31, 1.65)**	<0.00001
Blood glucose while delivery of the fetus (mmol/L)	1	54	MD: 0.00 (-0.17, 0.17)	1.00
Blood glucose while delivery of placenta(mmol/L)	1	54	**MD: -0.19 (-0.37, -0.01)**	0.04
Blood glucose about 2 hours after delivery of the fetus (mmol/L)	1	54	**MD: 0.90 (0.71, 1.09)**	<0.00001
Blood glucose about 6 hours after delivery of the fetus (mmol/L)	1	54	**MD: 1.11 (0.93, 1.29)**	<0.00001
Apgar scores <7	1	54	RR: 0.20 (0.01, 3.98)	0.29
Combined spinal and epidural analgesia: low dose sufentanil combined with bupivacaine VS bupivacaine				
Blood glucose while skin cutting (mmol/L)	1	66	**MD: -1.45 (-1.61, -1.29)**	<0.00001
Blood glucose while delivery of the fetus (mmol/L)	1	66	MD: 0.01 (-0.13, 0.15)	0.89
Blood glucose about 5 min after delivery of placenta (mmol/L)	1	66	**MD: 0.23 (0.06, 0.40)**	0.009
Blood glucose about 2 h after delivery of the fetus (mmol/L)	1	66	**MD: -0.89 (-1.07, -0.71)**	<0.00001

(*Continued*)

Appendix 1. (Continued).

Outcome	No. of studies	No. of participants	Effect estimate RR/MD (95%CI)	*P* value
Mean arterial pressure at 1min after anesthesia (mmHg)	1	66	MD: 0.40 (-2.11, 2.91)	0.75
Mean arterial pressure at 2 min after anesthesia (mmHg)	1	66	MD: 1.40 (-1.62, 4.42)	0.36
Mean arterial pressure at 5 min after anesthesia (mmHg)	1	66	**MD: 5.80 (3.12, 8.48)**	<0.00001
Mean arterial pressure at 10 min after anesthesia (mmHg)	1	66	MD: 0.30 (-2.47, 3.07)	0.83
Mean arterial pressure at 20 min after anesthesia (mmHg)	1	66	MD: 1.90 (-1.10, 4.90)	0.21
Apgar score at 1 min	1	66	MD: 0.10 (-0.17, 0.37)	0.46
Apgar score at 5 min	1	66	**MD: 0.10 (0.02, 0.18)**	0.01
Additional an antibiotic once vs. 24-h antibiotic application				
Marked effective rate	1	120	**RR: 0.68 (0.48, 0.97)**	<0.05
Effective rate	1	120	RR: 1.50 (0.97, 2.33)	>0.05
Inefficient rate	1	120	RR: 2.00 (0.38, 10.51)	>0.05
Total effective rate	1	120	RR: 0.97 (0.89, 1.05)	>0.05
WBC<12×10^9/L time (d)	1	120	MD: 0.50 (-0.02, 1.02)	>0.05
Body temperature (no fever and return to normal 48 h after surgery)	1	120	RR: 0.98 (0.93, 1.04)	>0.05
Class-A healing rate	1	120	RR: 0.97 (0.89, 1.05)	>0.05
Class-B healing rate	1	120	RR: 2.00 (0.38, 10.51)	>0.05
Class-C healing rate	1	120	-	>0.05

Notes: Bold values indicate statistical significance if the interval does not cross zero for continuous outcomes with MD , and cross one for dichotomous outcomes with RR. The bold values also mean the effect or difference was statistically significant.
Abbreviation: MD, mean difference.

Appendix 2. Summary of Evidence

Outcomes	No of participants(studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with control group	Risk difference with observation group
Insulin pump VS multiple subcutaneous injections of insulin					
Blood glucose standard time (d)	48 (1 RCT)	LOW [1,2]	-	-	**MD 5.3 fewer(5.78 fewer to 4.82 fewer)**
Dose of insulin (U/d)	48 (1 RCT)	LOW [1,2]	-	-	**MD 17 fewer(23.04 fewer to 10.96 fewer)**
Surgical incision healing time /d	48 (1 RCT)	LOW [1,2]	-	-	**MD 4.4 fewer(5.58 fewer to 3.22 fewer)**
Fasting and water-deprivation: short-term VS long-term					
Preoperative blood glucose (mmol/L)	162 (1 RCT)	LOW [1,2]	-	-	**MD 0.84 more(0.42 more to 1.26 more)**
Postoperative blood glucose (mmol/L)	162 (1 RCT)	LOW [1,5]	-	-	MD 0.16 more(0.17 fewer to 0.49 more)
Incidence of nausea	162 (1 RCT)	LOW [1,5]	RR 2.98(0.77 to 11.51)	62 per 1,000	15 more per 1,000(61 fewer to 152 more)
Incidence of vomiting	162 (1 RCT)	LOW [1,5]	RR 2.24(0.38 to 13.03)	21 per 1,000	26 more per 1,000(13 fewer to 248 more)
Incidence of neonatal hypoglycemia	162 (1 RCT)	LOW [1,5]	RR 0.25 (0.03 to 2.02)	62 per 1,000	47 fewer per 1,000(60 fewer to 63 more)
Incidence of preoperative hypoglycemia	162 (1 RCT)	LOW [1,5]	RR 0.54 (0.18 to 1.63)	113 per 1,000	52 fewer per 1,000(93 fewer to 71 more)
Maternal anal discharge time(h)	162 (1 RCT)	LOW [1,5]	-	-	MD 0.04 fewer(0.25 fewer to 0.17 more)
Bleeding during childbirth (ml)	162 (1 RCT)	LOW [1,2]	-	-	**MD 42.71 fewer (82.55 fewer to 2.86 fewer)**
Neonatal Apgar scores at 1 min	162 (1 RCT)	LOW [1,5]	-	-	MD 0.03 more(0.18 fewer to 0.24 more)
Neonatal Apgar scores at 5 min	162 (1 RCT)	LOW [1,5]	-	-	MD 0.03 fewer(0.14 fewer to 0.08 more)
Postnatal blood glucose (mmol/L)	162 (1 RCT)	LOW [1,5]	-	-	MD 0.45 more(0.03 fewer to 0.87 more)
Health education: individualization VS convention					
Fasting blood glucose compliance rate	110 (1 RCT)	LOW [1,5]	RR 1.08(0.86 to 1.35)	764 per 1,000	61 more per 1,000(107 fewer to 267 more)
Glucose-target-rate at 2 o'clock	110 (1 RCT)	LOW [1,2]	**RR 1.31(1.04 to 1.66)**	836 per 1,000	**259 more per 1,000 (33 more to 552 more)**
Glucose-target-rate at 0 o'cl	110 (1 RCT)	LOW [1,2]	**RR 1.23(1.01 to 1.50)**	873 per 1,000	**201 more per 1,000 (9 more to 436 more)**
Nursing service satisfaction	110 (1 RCT)	LOW [1,2]	-	-	**MD 6.51 more(5.80 more to 7.22 more)**

(*Continued*)

Appendix 2. (Continued).

Outcomes	No of participants(studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with control group	Risk difference with observation group
Fructose Injection vs. Glucose Injection + Insulin					
Blood glucose level at 1.5~2 h after infusion (mmol/L)	202 (2 RCTs)	LOW [2,3]	-	-	**MD 1.17 fewer(1.93 fewer to 0.41 fewer)**
Blood glucose level at 3~4 h after infusion (mmol/L)	202 (2 RCTs)	LOW [2,3]	-	-	**MD 0.99 fewer(1.61 fewer to 0.36 fewer)**
Blood glucose level at 6h after infusion (mmol/L)	70 (1 RCT)	LOW [4,5]	-	-	MD 0.62 fewer(1.86 fewer to 0.61 more)
Insulin level at 1.5 h after infusion (mU/L)	132 (1 RCT)	LOW [2,4]	-		**MD 13.5 fewer (19.02 fewer to 7.98 fewer)**
Insulin level at 3 h after infusion (mU/L)	132 (1 RCT)	LOW [2,4]	-		**MD 8.59 fewer (13.75 fewer to 3.43 fewer)**
Blood uric acid level at 3 h after infusion (μmol/L)	132 (1 RCT)	LOW [4,5]	-		MD 8 fewer(34.96 fewer to 18.96 more)
Positive rate of urine carcass	202 (2 RCTs)	LOW [3,5]	OR 1.14(0.49 to 2.64)	129 per 1,000	15 more per 1,000(61 fewer to 152 more)
Positive rate of urine glucose	70 (1 RCT)	LOW [1,5]	RR 0.21(0.01 to 4.25)	56 per 1,000	44 fewer per 1,000(55 fewer to 181 more)
PCEA VS PCIA					
Blood glucose level at 3 h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,5]	-	-	MD 0.01 more(0.21 fewer to 0.23 more)
Blood glucose level at 3 h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,2]	-	-	**MD 0.8 fewer(1.01 fewer to 0.59 fewer)**
Blood glucose level at 12h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,2]	-	-	**MD 0.76 fewer(1 fewer to 0.52 fewer)**
Blood glucose level at 24h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,2]	-		**MD 0.65 fewer(0.87 fewer to 0.43 fewer)**
Blood glucose level at 36h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,2]	-	-	**MD 0.75 fewer(0.96 fewer to 0.54 fewer)**
VAS score at 36h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,5]	-	-	MD 0.04 fewer(0.31 fewer to 0.23 more)
VAS score at 6h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,5]	-		MD 0.01 fewer(0.2 fewer to 0.18 more)
VAS score at 12h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,5]	-		MD 0.02 fewer(0.24 fewer to 0.2 more)
VAS score at 24h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,5]	-		MD 0.05 fewer(0.39 fewer to 0.29 more)
VAS score at 36h after the onset of analgesia (mmol/L)	33 (1 RCT)	LOW [1,5]	-		MD 0.04 fewer(0.35 fewer to 0.27 more)
Satisfaction rate of analgesic effect	33 (1 RCT)	LOW [1,5]	RR 1.00(0.89 to 1.12)	1,000 per 1,000	**0** fewer per 1,000(110 fewer to 120 more)

(*Continued*)

Appendix 2. (Continued).

Outcomes	No of participants(studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with control group	Risk difference with observation group
Vausea and vomiting	33 (1 RCT)	LOW [1,5]	RR 0.31(0.01 to 7.21)	63 per 1,000	43 fewer per 1,000(62 fewer to 388 more)
Uroschesis	33 (1 RCT)	LOW [1,5]	RR 2.83(0.12 to 64.89)	-	-
Postoperative wound care: microwave treatment of VS routine care					
Wound healing rate at first stage	140 (1 RCT)	LOW [1,2]	**RR 1.15(1.03 to 1.29)**	843 per 1,000	**126 more per 1,000 (25 more to 244 more)**
Psychological intervention (including music therapy) VS routine care					
Systolic pressure immediately into the operating room (mmHg)	200 (1 RCT)	LOW [2,6]	-	-	**MD 9.8 fewer(12.42 fewer to 7.18 fewer)**
Systolic pressure after surgery into the operating room 30min (mmHg)	200 (1 RCT)	LOW [2,6]	-	-	**MD 35.37 fewer (38.32 fewer to 32.42 fewer)**
Intraoperative systolic pressure (mmHg)	153 (1 RCT)	LOW [2,6]	-	-	**MD 22.63 fewer (27.24 fewer to 18.02 fewer)**
Diastolic pressure immediately into the operating room (mmHg)	200 (1 RCT)	LOW [2,6]	-	-	**MD 3.58 fewer(5.2 fewer to 1.96 fewer)**
Diastolic pressure after surgery into the operating room 30min (mmHg)	200 (1 RCT)	LOW [2,6]	-	-	**MD 7.58 fewer(9.62 fewer to 5.54 fewer)**
Intraoperative diastolic pressure (mmHg)	153 (1 RCT)	LOW [2,6]	-	-	**MD 10.61 fewer (14.65 fewer to 6.57 fewer)**
Heart rate immediately into the operating room	200 (1 RCT)	LOW [5,6]	-	-	MD 0.86 fewer(2.69 fewer to 0.97 more)
Heart rate after surgery into the operating room 30min	200 (1 RCT)	LOW [2,6]	-	-	**MD 8.89 fewer (10.52 fewer to 7.26 fewer)**
Anxiety score immediately into the operating room	200 (1 RCT)	LOW [5,6]	-	-	MD 0.13 fewer(2.57 fewer to 2.31 more)
Anxiety score after surgery into the operating room 30min	200 (1 RCT)	LOW [2,6]	-	-	**MD 2.22 fewer(3.55 fewer to 0.89 fewer)**
Intro-operative hemorrhage (ml)	153 (1 RCT)	LOW [2,6]	-	-	**MD 62.39 fewer (78.31 fewer to 46.47 fewer)**
Postoperative pains	153 (1 RCT)	LOW [2,6]	**RR 0.73(0.60 to 0.89)**	855 per 1,000	**231 fewer per 1,000 (342 fewer to 94 fewer)**

(*Continued*)

Appendix 2. (Continued).

Outcomes	No of participants(studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with control group	Risk difference with observation group
Postoperative normal feeding	153 (1 RCT)	LOW [5,6]	RR 1.07(0.99 to 1.16)	908 per 1,000	64 more per 1,000(9 fewer to 145 more)
Postoperative morbidity	153 (1 RCT)	LOW [2,6]	**RR 0.35(0.19 to 0.64)**	408 per 1,000	**265 fewer per 1,000 (330 fewer to 147 fewer)**
Epidural anesthesia vs general anesthesia					
Blood glucose while skin cutting (mmol/L)	54 (1 RCT)	LOW [1,2]	-	-	**MD 1.48 higher (1.31 higher to 1.56 higher)**
Blood glucose while delivery of the fetus (mmol/L)	54 (1 RCT)	LOW [1,5]	-	-	MD **0** (0.17 lower to 0.17 higher)
Blood glucose while delivery of placenta(mmol/L)	54 (1 RCT)	LOW [1,2]	-	-	**MD 0.19 fewer(0.37 fewer to 0.1 fewer)**
Blood glucose about 2 hours after delivery of the fetus (mmol/L)	54 (1 RCT)	LOW [1,2]	-	-	**MD 0.9 higher(0.71 higher to 1.09 higher)**
Blood glucose about 6 hours after delivery of the fetus (mmol/L)	54 (1 RCT)	LOW [1,2]	-	-	**MD 1.11 higher (0.93 higher to 1.29 higher)**
Apgar scores <7	54 (1 RCT)	LOW [1,5]	RR 0.20(0.01 to 3.98)	-	-
Combined spinal and epidural analgesia: low dose sufentanil combined with bupivacaine VS bupivacaine					
Blood glucose while skin cutting (mmol/L)	66 (1 RCT)	LOW [1,2]	-	-	**MD 1.45 fewer(1.61 fewer to 1.29 fewer)**
Blood glucose while delivery of the fetus (mmol/L)	66 (1 RCT)	LOW [1,5]	-	-	MD 0.01 more(0.13 fewer to 0.15 more)
Blood glucose about 5min after delivery of placenta (mmol/L)	66 (1 RCT)	LOW [1,2]	-	-	**MD 0.23 more(0.06 more to 0.4 more)**
Blood glucose about 2 hours after delivery of the fetus (mmol/L)	66 (1 RCT)	LOW [1,2]	-	-	**MD 0.89 fewer(1.07 fewer to 0.71 fewer)**
Mean arterial pressure at 1min after anesthesia (mmHg)	66 (1 RCT)	LOW [1,5]	-	-	MD 0.4 more(2.11 fewer to 2.91 more)
Mean arterial pressure at 2min after anesthesia (mmHg)	66 (1 RCT)	LOW [1,5]	-	-	MD 1.4 more(1.62 fewer to 4.42 more)
Mean arterial pressure at 5min after anesthesia (mmHg)	66 (1 RCT)	LOW [1,2]	-	-	**MD 5.8 more(3.12 more to 8.48 more)**
Mean arterial pressure at 10min after anesthesia (mmHg)	66 (1 RCT)	LOW [1,5]	-	-	MD 0.3 more(2.47 fewer to 3.07 more)
Mean arterial pressure at 20min after anesthesia (mmHg)	66 (1 RCT)	LOW [1,5]	-	-	MD 1.9 more(1.1 fewer to 4.9 more)

(*Continued*)

Appendix 2. (Continued).

Outcomes	No of participants(studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with control group	Risk difference with observation group
Apgar score at 1min	66 (1 RCT)	LOW [1,5]	-	-	MD 0.1 more(0.17 fewer to 0.37 more)
Apgar score at 5mins	66 (1 RCT)	LOW [1,2]	-	-	**MD 0.1 more(0.02 more to 0.18 more)**
Additional an antibiotic once vs 24 hours antibiotic application					
Marked effective rate	120 (1 RCT)	LOW [1,2]	**RR 0.68(0.48 to 0.97)**	633 per 1,000	**203 fewer per 1,000 (329 fewer to 19 fewer)**
Effective rate	120 (1 RCT)	LOW [1,5]	RR 1.50(0.97 to 2.33)	333 per 1,000	167 more per 1,000(10 fewer to 443 more)
Inefficient rate	120 (1 RCT)	LOW [1,5]	RR 2.00(0.38 to 10.51)	33 per 1,000	33 more per 1,000(21 fewer to 317 more)
Total effective rate	120 (1 RCT)	LOW [1,5]	RR 0.97(0.89 to 1.05)	967 per 1,000	29 fewer per 1,000 (106 fewer to 48 more)
WBC<12×10^9/L time (d)	120 (1 RCT)	LOW [1,5]	-	-	MD 0.50 more(0.02 fewer to 1.02 more)
Body temperature (no fever and return to normal 48 h after surgery)	120 (1 RCT)	LOW [1,5]	RR 0.98(0.93 to 1.04)	983 per 1,000	20 fewer per 1,000(69 fewer to 39 more)
Class-A healing rate	120 (1 RCT)	LOW [1,5]	RR 0.97(0.89 to 1.05)	967 per 1,000	29 fewer per 1,000 (106 fewer to 48 more)
Class-B healing rate	120 (1 RCT)	LOW [1,5]	RR 2.00(0.38 to 10.51)	33 per 1,000	33 more per 1,000(21 fewer to 317 more)
Class-C healing rate	120 (1 RCT)	-	-	-	-

*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

GRADE Working Group grades of evidence: high quality: we are very confident that the true effect lies close to that of the estimate of the effect. **Moderate quality**: we are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. **Low quality**: our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. **Very low quality**: we have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Notes: [1]No random sequences were reported to generate and assign hidden methods, and no blindness was given to researchers, subjects, and outcome evaluators. [2]The sample size is less than the optimal information sample size. [3]None of the studies reported randomized generation and allocation of hidden methods, one of which did not blind the researchers and subjects. [4]The method of generating and assigning hidden random numbers is not reported. [5]The sample size is less than the optimal information sample size, and the confidence interval of the combined effect is across the invalid line. [6]No evaluation of the outcome of the blind. The bold values mean the effect or difference was statistically significant.
Abbreviation: MD, mean difference.