

ORIGINAL RESEARCH



Mapping theme trends and knowledge structure of labor analgesia: a quantitative, co-word biclustering analysis of data in 2000-2020

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Abstract

Background: The distribution knowledge structure and pattern of the literature on labor analgesia in PubMed were examined.

Methods: Scientific papers on labor analgesia published from 1 January, 2000 to 31 June, 2020 were retrieved. The extracted MeSH items were quantitatively analyzed by the Bibliographic Item Co-Occurrence Matrix Builder (BICOMB), and the high frequency MeSH items were identified. In gCLUTO software, repeated bisection method was used to Mountain visualisation, and the visual matrix was established. By constructing high-frequency MeSH terms co-occurrence matrix, strategic diagram and social network are further completed.

Results: The search strategy yielded 2870 papers, and the number of papers published annually had changed slightly during the study period. Among all extracted MeSH terms, 42 high-frequency MeSH terms were identified by consensus, and were divided into six categories by diclustering analysis. In the strategic diagram, the methods of labor analgesia, drug doses, and routes of administration were properly presented. In contrast, statistical and numerical data on obstetric analgesia were relatively underdeveloped, and management of pain during labor was undeveloped. In the social network analysis, the position status of each component was determined by the centrality values.

Conclusions: The findings on labor analgesia are relatively divergent, and the six research categories outlined in this study reflect the publication trends in the field of labor analgesia to some extent. Our quantitative bibliometric research across a 20-year span depicts the overall direction of the latest topics and provides some hints for researchers when launching new projects.

Keywords

Labor analgesia; Bibliometric analysis; Co-word analysis; Social network analysis

1. Background

The American College of Obstetrics and Gynecology (ACOG) pointed out that it was inhumane and unhealthy for women to suffer during childbirth [1, 2]. The intense pain of childbirth can activate the sympathetic nervous system, increase the secretion of catecholamines, which cause a decrease in uterine blood flow and an increase in cardiac output and blood pressure [3]. Hyperventilation during contractions may cause respiratory alkalosis and left shift of oxygenated hemoglobin curve, reducing the oxygen supply to the fetus. In addition, fear and anxiety can aggravate labor pain, leading to an increase in the rate of cesarean section [4]. Women should be helped to give birth with smiles and joy instead of moaning, painful and struggling. The purpose of labor analgesia is to reduce labor pain and anxiety, and improve labor comfort and satisfaction [5, 6]. However, there are so many choices for labor analgesia,

and the impact of labor analgesia on the safety of mothers and babies, on labor process, contractions, intrapartum fever and postpartum depression are still controversial [5]. According to the bibliometric analysis method, our studies use cluster visualization analysis to show the thematic structure of childbirth analgesia; the strategic coordinates to show the importance and characteristics of each research topic in the overall disciplinary structure; the social network map to show the internal relations of the topics. The study summarizes the research hotspots and development trends of labor analgesia in the past 20 years, so as to facilitate researchers in this discipline to understand the frontiers of the discipline, further clarify their research goals, rationally plan the discipline layout, adjust the research direction, and concentrate limited strength in key areas.

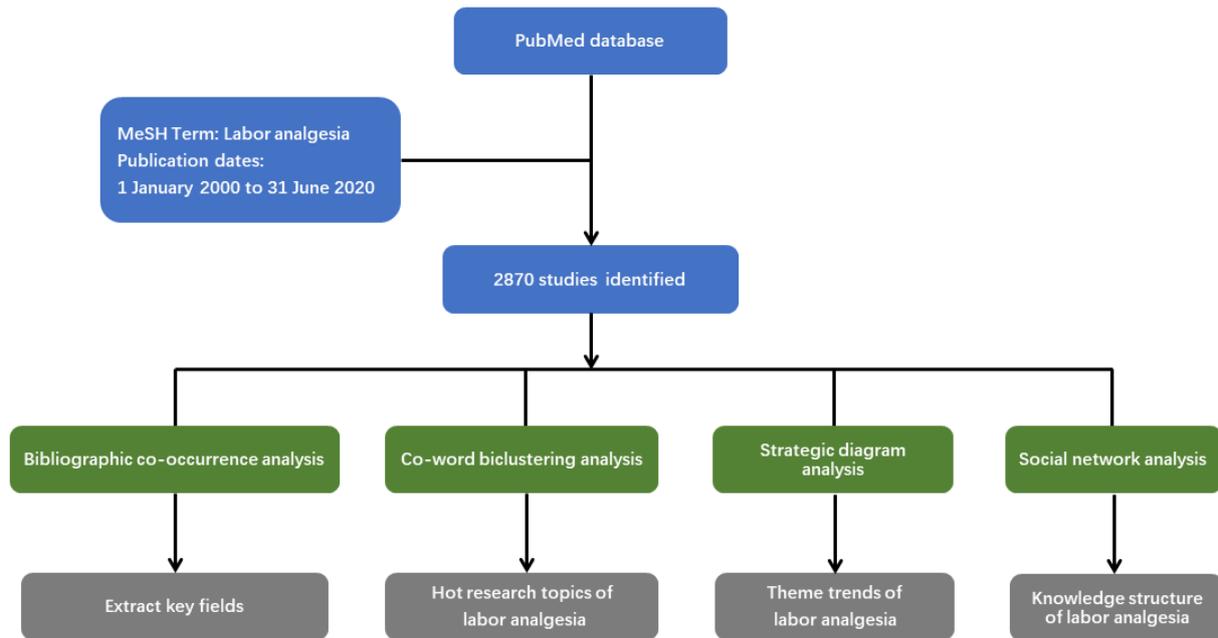


FIGURE 1. The flowchart of literature selection.

2. Data and methods

2.1 Data resource and search strategy

In PubMed database of the US National Center for Biotechnology Information, Medical Subject Heading (MeSH) is used for indexing, cataloging, and searching for biomedical and health-related information which created by the National Library of Medicine. We retrieved and downloaded the data by using MeSH term as the retrieval category. The retrieval term was set as “Labor analgesia” [MeSH]. A total of 2870 articles published between 1 January 2000 and 31 June 2020 were retrieved. The data were saved in XML format including title, author, country, MeSH terms, and publication year of each study. The specific flowchart is shown in Fig. 1.

2.2 Data extraction and bibliographic matrix building

The required data were extracted from the PubMed database. Two investigators (Zhang and Bai) independently conducted the primary search by screening the full texts, titles and, in some cases, abstracts, of the studies. The agreement rate between them was 0.90, which indicated strong agreement [7]. Differences, if any, were discussed. The co-occurring matrices and term-source article relationships were checked using the Bibliographic Item Co-Occurrence Matrix Builder (BICOMB) software developed by Professor Cui of the China Medical University that is available freely online [8]. BICOMB was utilized to analyze the contribution characteristics of country, journal, year of publication, and main/subheadings MeSH terms. In addition, the numbers of high-frequency main MeSH terms/subheadings were defined by the H index.

2.3 MeSH terms Biclustering analysis

Biclustering analysis was performed on high-frequency main MeSH terms/subheadings and PubMed Unique Identifiers of the labor analgesia-related studies. The main MeSH terms/subtitles were classified according to the term-source article matrix. Repeated bisection method is used in gCLUTO software to visualize mountain body and establish visualization matrix. The peaks in the three-dimensional (3D) terrain were marked by numbers, representing the clusters analysed by biclustering. The data of the associated clusters are reflected by the colour, height, volume and position of the peaks, and the relative position of each peak is the most informative attribute in the figure. The height of each peak represents the internal resemblance of a cluster, the distance between peaks reflects the correlation between clusters and the volume of the peak is proportional to the number of main MeSH terms/subheadings. In addition, the peak colour is the internal standard deviation of the objects in the cluster, and blue is high deviation, red is low. Based on the results of the biclustering analysis, the structures related to the research focus areas were further analysed.

2.4 Strategic diagram analysis

Taking theme centrality and density as axes, we constructed a two-dimensional strategy diagram. The horizontal axis represented the centrality, and the vertical axis represented the density. The Centrality referred to the intensity of interaction between domains, and the density referred to the intensity of internal connection in a certain field. The coordinates were divided into four quadrants by two axes, and we used strategic diagram calculation formula to distribute the results of the subject words main MeSH terms/subheadings to four quadrants.

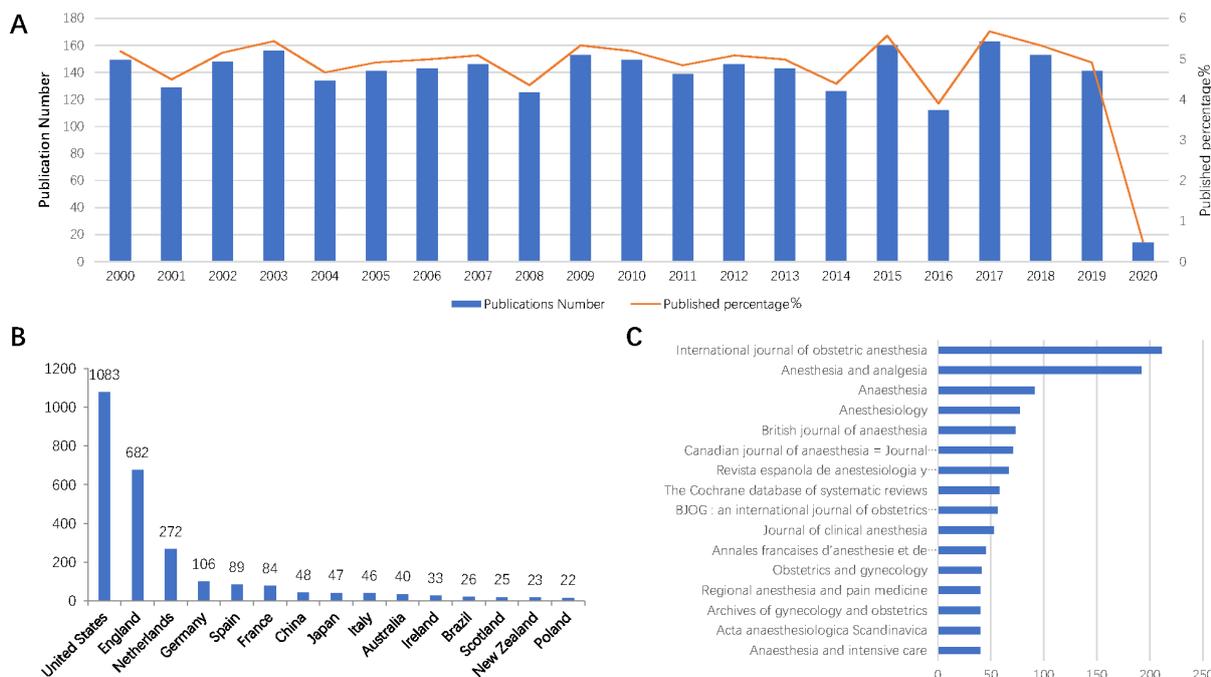


FIGURE 2. Characteristics of labor analgesia-related publications. Publication years (A), publication contrary (B) and high frequently journals (C).

2.5 Social network analysis

Ucinet 6.0 software was used to draw the social network analysis network by analyzing the co-occurrence matrix of high-frequency main MeSH terms/subheadings. Then social network analysis revealed the intrinsic link of labor analgesia. With NetDraw 2.084 software, the main MeSH terms/subheadings was to be submitted and visualised into a two-dimensional network. In the network, each node represented a main MeSH terms/subheadings, and each link represented co-occurrence frequency. The tightness of the network was respected by calculating the keyword density. We measured three centralities of MeSH terms/subheadings (closeness, betweenness, and degree) to compare the positions of different nodes in the structure of labor analgesia network.

3. Results

The search strategy yielded a total of 2870 publications that were included in this study. The data on labor analgesia-related publications in the designated study period are shown in Fig. 2-A. The highest number of articles on labor analgesia was published in the United States, accounting for 37.73% of all the retrieved studies, followed by England and the Netherlands (Fig. 2-B). The top ranking 15 journals are shown in Fig. 2-C. The *International Journal of Obstetric Anesthesia* published the highest number of labor analgesia-related articles (211, 7.34%), followed by *Anesthesia and Analgesia* (192, 6.68%) and *Anesthesia* (91, 3.16%).

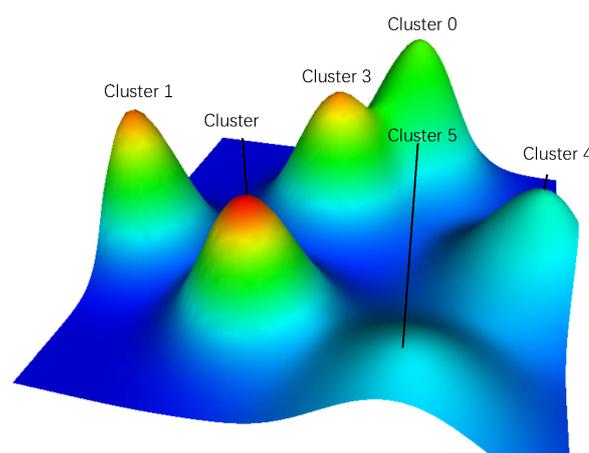


FIGURE 3. A visualized mountain map biclustering of major MeSH terms with high frequency and articles on Labor Analgesia.

3.1 Research hot spots according to MeSH term clusters

Among the labor analgesia-related publications, high-frequency main MeSH terms/subheadings had a cumulative frequency of 43.40% and were the hot research topics over the past 20 years. The high-frequency main MeSH terms/subheadings were analysed, and six clusters were identified by biclustering analysis. Accordingly, 41 high-frequency main MeSH terms/subheadings were classified into six clusters (Fig. 3). The hierarchical trees on the left and top sides represent the high-frequency main MeSH terms/subheadings and PubMed Unique Identifier (PMID), respectively. Furthermore, the themes in the representative

TABLE 1. Highly Frequent Terms in Labor Analgesia.

Rank	main MeSH terms/MeSH subheadings	Frequency	Proportion of frequency (%)	Cumulative percentage (%)
1	Analgesia, Obstetrical/methods	667	5.2516	5.2516
2	Analgesia, Obstetrical	448	3.5273	8.7788
3	Analgesia, Epidural	411	3.2360	12.0148
4	Analgesia, Epidural/methods	406	3.1966	15.2114
5	Analgesia, Epidural/adverse effects	338	2.6612	17.8726
6	Analgesia, Obstetrical/adverse effects	337	2.6533	20.5259
7	Labor, Obstetric	270	2.1258	22.6518
8	Labor Pain/drug therapy	251	1.9762	24.6280
9	Analgesics, Opioid/administration & dosage	179	1.4093	26.0373
10	Anesthetics, Local/administration & dosage	173	1.3621	27.3994
11	Labor Pain/therapy	114	0.8976	28.2970
12	Bupivacaine/administration & dosage	99	0.7795	29.0765
13	Analgesia, Patient-Controlled/methods	97	0.7637	29.8402
14	Labor, Obstetric/drug effects	92	0.7244	30.5645
15	Analgesia, Epidural/statistics & numerical data	84	0.6614	31.2259
16	Analgesia, Obstetrical/statistics & numerical data	82	0.6456	31.8715
17	Delivery, Obstetric/methods	79	0.6220	32.4935
18	Analgesia/methods	78	0.6141	33.1076
19	Anesthesia, Obstetrical/methods	78	0.6141	33.7218
20	Analgesia, Patient-Controlled	76	0.5984	34.3201
21	Fentanyl/administration & dosage	76	0.5984	34.9185
22	Delivery, Obstetric	73	0.5748	35.4933
23	Cesarean Section/statistics & numerical data	66	0.5196	36.0129
24	Amides/administration & dosage	66	0.5196	36.5326
25	Analgesics, Opioid/therapeutic use	63	0.4960	37.0286
26	Analgesics, Opioid/adverse effects	63	0.4960	37.5246
27	Cesarean Section	62	0.4882	38.0128
28	Transcutaneous Electric Nerve Stimulation/methods	61	0.4803	38.4930
29	Pain Management/methods	61	0.4803	38.9733
30	Labor, Obstetric/physiology	59	0.4645	39.4378
31	Piperidines/administration & dosage	57	0.4488	39.8866
32	Anesthesia, Obstetrical	51	0.4015	40.2882
33	Pain/prevention & control	47	0.3700	40.6582
34	Pain Management	45	0.3543	41.0125
35	Labor, Obstetric/psychology	45	0.3543	41.3668
36	Sufentanil/administration & dosage	45	0.3543	41.7211
37	Pain, Postoperative/drug therapy	44	0.3464	42.0676
38	Labor Pain/psychology	44	0.3464	42.4140
39	Transcutaneous Electric Nerve Stimulation	42	0.3307	42.7447
40	Pain/drug therapy	42	0.3307	43.0753
41	Anesthesia, Spinal	41	0.3228	43.3982

papers in each cluster were summarised. Considering the hot research topics based on MeSH term clusters, the cumulative frequency of the 41 high-frequency main MeSH

terms/subheadings was 43.3982% (Table 1).

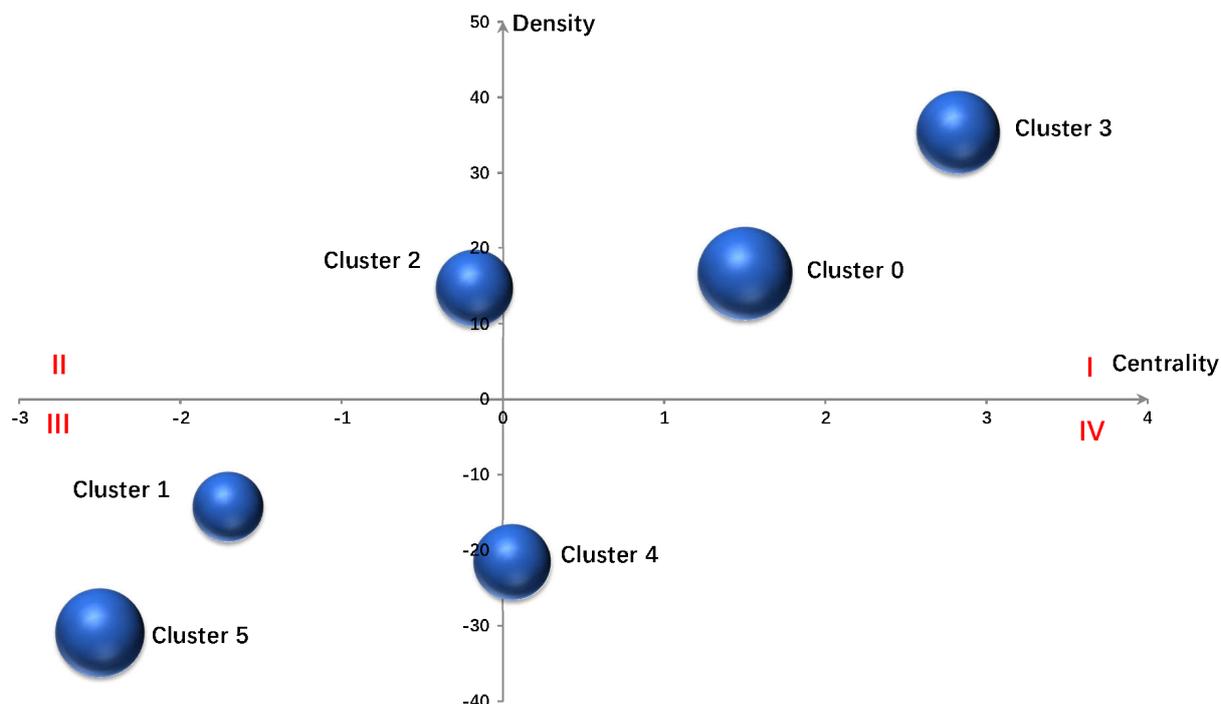


FIGURE 4. Strategic diagram for Labor Analgesia. Cluster No. 0, 3 locate in Quadrant I, representing that researches on analgesia methods, administration and dosage are in the core status with high density and centrality. Cluster No. 2 locate in Quadrant II, representing that researches on labor analgesia related to adverse effects are in the peripheral and developed status. Cluster No. 1, 5 locate in Quadrant III, indicating that researches on statistics and numerical data, as well as psychology related studies on labor analgesia are not mature at the edge of the research field. Cluster No. 4 locate in Quadrant IV, indicating that researches on pain management are in the central and undeveloped status.

3.2 Strategic diagram for labor analgesia

Quadrant I (upper-right) represents motor themes with strong centrality and high density. Quadrant II (upper-left) represents specialised themes with high density, but inadequate external interactions. Quadrant III (lower-left) contains themes with low density and inadequate centrality, and these themes may be marginal topics. Quadrant IV (lower-right) contains themes with strong centrality but lacking internal maturation. In the strategic diagrams, the themes are represented by spheres of different sizes, which are organised in different quadrants according to their internal and external cohesion (density and centrality).

As shown in Fig. 4, the area of the spheres is proportional to the number of high-frequency main MeSH terms/subheadings. Cluster No. 0 and 3 are located in Quadrant I, indicating that studies on analgesia methods, administration, and dosage are in the core position with high density and centrality. Cluster No. 2 is located in Quadrant II, indicating that research on labor analgesia related to adverse effects is in the peripheral and developed position. Cluster No. 1 and 5 are located in Quadrant III, indicating that statistical, numerical, and psychology-related studies on labor analgesia are not mature and at the edge of the research field. Cluster No. 4 is located in Quadrant IV, indicating that research on pain management is in the central and undeveloped position. The strategic diagram shows the development and trends in each cluster over the past 20 years.

3.3 Social network analysis of labor analgesia

The density value of labor analgesia-related studies was 0.6244. This indicates that the overall structure of the network is relatively close. Degree, closeness, and betweenness were used as centrality parameters to build the social network analysis network (Fig. 5 and Table 2).

In the network of labor analgesia studies published in the last 20 years, 20 main MeSH terms/subheadings had a high degree of centrality, including the top 15 high-frequency ones. “Analgesia, Obstetrical/methods” had the highest degree of centrality and betweenness centrality. It played the most significant mediating role in the network. “Analgesia, Epidural” and “Analgesia, Obstetrical” also had high betweenness centrality, indicative of their prominent mediating roles in the network. The mean betweenness centrality was 7.512 ± 7.396 (Table 3).

4. Discussion

MeSH terms can reveal the content of studies, research status, and trends in different disciplines. According to the analytical results obtained from the BICOMB software, the distribution characteristics of the “Labor Analgesia” [MeSH] literature in the last 20 years maintained a horizontal trend, with a slight decrease in 2016. Our analysis showed that the United States and the United Kingdom were the largest contributors, which can be explained by the fact that English is the first language

TABLE 2. Individual centrality of Labor Analgesia research.

Rank	main MeSH terms/subheadings	Degree	Betweenness	Closeness
1	Analgesia, Obstetrical/methods	39	34.416	41
2	Labor, Obstetric	36	28.287	44
3	Labor Pain/drug therapy	35	12.818	45
4	Analgesia, Epidural/methods	35	17.379	45
5	Analgesia, Epidural/adverse effects	35	13.426	45
6	Analgesia, Epidural	34	19.052	46
7	Analgesia, Obstetrical/adverse effects	33	10.737	47
8	Analgesics, Opioid/administration & dosage	32	7.815	48
9	Anesthetics, Local/administration & dosage	32	8.927	48
10	Labor, Obstetric/drug effects	32	9.92	48
11	Analgesia, Obstetrical	31	17.757	49
12	Analgesia, Patient-Controlled	29	6.719	51
13	Delivery, Obstetric	29	9.004	51
14	Analgesia, Patient-Controlled/methods	28	6.764	52
15	Pain Management/methods	28	14.318	52
16	Labor, Obstetric/physiology	27	5.843	53
17	Labor Pain/therapy	25	13.179	55
18	Fentanyl/administration & dosage	25	3.104	55
19	Bupivacaine/administration & dosage	25	3.189	55
20	Piperidines/administration & dosage	25	3.656	55
21	Cesarean Section/statistics & numerical data	24	3.569	56
22	Amides/administration & dosage	24	2.905	56
23	Sufentanil/administration & dosage	24	2.818	56
24	Analgesia, Obstetrical/statistics & numerical data	24	4.196	56
25	Pain/prevention & control	23	6.786	57
26	Anesthesia, Obstetrical/methods	23	3.048	57
27	Cesarean Section	22	2.51	58
28	Analgesia/methods	22	10.076	58
29	Analgesics, Opioid/therapeutic use	22	2.609	58
30	Anesthesia, Spinal	22	2.728	58
31	Delivery, Obstetric/methods	21	2.309	59
32	Pain/drug therapy	21	4.079	59
33	Analgesics, Opioid/adverse effects	20	1.306	60
34	Anesthesia, Obstetrical	20	2.619	60
35	Pain, Postoperative/drug therapy	19	2.281	61
36	Labor Pain/psychology	18	2.643	62
37	Analgesia, Epidural/statistics & numerical data	18	1.788	62
38	Labor, Obstetric/psychology	16	1.088	64
39	Pain Management	11	1.81	69
40	Transcutaneous Electric Nerve Stimulation	9	0.421	71
41	Transcutaneous Electric Nerve Stimulation/methods	6	0.1	74

PCEA alone, but increased instrument-assisted delivery rates and prolonged second labor [20]. Recently, programmed intermittent epidural bolus (PIEB) has been used, which can

be regularly administered by pulse. It not only brings analgesic drugs in full contact with the spinal nerve in the epidural cavity during each pulse administration but also provides the next

TABLE 3. Descriptive statistics for centrality measure about Labor Analgesia.

Centralization	MeanSD	Min	Max	Network centralization (%)
Degree	24.976 ± 7.253	6.000	39.000	36.86
Betweenness	7.512 ± 7.396	0.100	34.416	3.54
Closeness	55.024 ± 7.253	41.000	74.000	49.01

pulse administration before the drug action from the last pulse disappears, providing a sustained and stable analgesic effect. PIEB significantly increased maternal satisfaction compared with CEI, and reduced the incidence of pain outbreak, movement block, instrument-assisted birth, analgesic drug dosage, and PCEA [21, 22]. Foreign authors Leo [23] and Patkar [24] *et al.* conducted comparative studies with PIEB and CEI groups and found that the analgesic effect in the two groups was similar. Leo [23] stated that the consumption of anaesthetic drugs per unit time in the PIEB group was also lower than that in the CEI group, and the onset time in the PIEB group was also relatively fast. In addition, computer-integrated patient-controlled epidural analgesia (CIPCEA) is an effective method of providing labor analgesia by automatically adjusting the injection rate according to the needs of the woman, thus reducing the incidence of pain outbreaks, the use of local anaesthetics, and the workload of the anaesthesiologist [25].

Cluster 2 is related to adverse reactions to labor analgesia. Most studies have not reported rare or severe adverse events associated with epidural labor analgesia [26]. Low-dose opioid analgesics combined with local anaesthetics are commonly used in spinal anaesthesia, but opioids often lead to a series of adverse reactions such as nausea, vomiting, itchy skin, fever, foetal tachycardia, urinary retention, neonatal respiratory depression, and others [24, 27]. ElKerdawy [28, 29] stated that epidural labor analgesia can cause postpartum hypotension in women with preeclampsia; Shanbin *et al.* [17] pointed out that in addition to the side effects caused by opioids, epidural labor analgesia also led to back pain (10%) and chills (5%) in women and bradycardia in new-borns (10%). Second, intrapartum fever is also a common complication of labor analgesia. The causes of disease may be related to the changes in maternal body temperature regulation function, the increase in obstetric heat, the high ambient temperature in the delivery room, and the differences in maternal population and obstetric management approaches. Other studies have suggested that the main mechanism may be non-infectious inflammation, such as an increase in serum interleukin-6 level [22]. Of note, Pavithra *et al.* [30] pointed out that epidural analgesia is an invasive operation, and the incidence of headache (87.0% vs. 8.7%, $P < 0.001$), low back pain (47.2% vs. 19.6%, $P = 0.002$), neck pain (30.1% vs. 2.2%, $P < 0.001$), hearing problems (13.8% vs. 0, $P = 0.02$), and visual symptoms (19.5% vs. 0, $P = 0.002$) is higher in puerperas after a dural puncture accident than in normal puerperas. The data indicate that long-term complications of analgesia puncture require attention.

Clusters 1 and 5 represented statistical and numerical data on obstetric analgesia. Many studies have suggested that epidural analgesia is initiated when the cervix is opened to ≥ 3 cm, and epidural analgesia is stopped when the cervix is fully opened. However, in these cases, the duration of epidural analgesia was

short and satisfaction was low. Emerging maternal data are changing previous perceptions. Wong *et al.* [31] showed that, compared with intravenous analgesia, intra-spinal analgesia at early labor (cervix dilation < 4 cm) did not increase the caesarean section rate, and the analgesia was effective, and the labor process was shortened. A randomised, controlled study involving 12,793 women [32] showed that epidural analgesia during the incubation period of labor (dilation of the cervix ≥ 1 cm) did not prolong labor compared with active labor (cervix ≥ 4 cm) nor did it increase the caesarean section rate. Other studies showed that discontinuing epidural analgesia close to the time of the opening of the cervix does not reduce the rate of instrumentally assisted delivery but increases the incidence of second-stage hypoanalgesia [33]. The effect of epidural labor analgesia on labor process is still controversial in Academia. In addition, differences among ethnicities, midwifery techniques, and medical expertise may have different effects on the interpretation and treatment of labor pain. Therefore, high-quality, large-sample prospective randomised controlled trials are needed to confirm all above clinically [34].

Cluster 4 represents the management of pain during labor. It has been found that the expression of μ opioid receptor genes is related to pain sensitivity and can affect the analgesic effect of labor analgesia. A meta-analysis found that fentanyl ED50 was significantly lower in women with homozygous and heterozygous GJJ8 alleles than in women with homozygous wild-type A118 alleles who received epidural labor analgesia [35]. A similar study found that women with homozygous and heterozygous G118 alleles were 1.25 times more likely to receive sufentanil epidural analgesia than women with the wild-type A118 allele [36]. However, some studies have found that the presence or absence of the G allele does not affect the analgesic effect of opioids during epidural delivery [37]. In addition, epidural injections of clonidine and neostigmine significantly prolonged analgesia and reduced the rate of hourly local anaesthetic and opioid use. There was no significant difference between the two drugs in total labor time, delivery mode (caesarean section or device-assisted delivery rate), and neonatal Apgar score, and no significant adverse reactions were found [38].

Amounts of studies has shown that epidural labor analgesia is safe and effective, and the incidence of maternal and infant adverse reactions is low [2]. At present, it is still the mainstream method of labor analgesia. Although this study focuses on research hotspots and future research trends of labor analgesia, it also has its own limitations. For example, in the data analysis, only high-frequency words are selected as the analysis object, and data with low frequency are ignored, which will lead to certain errors in the research results. In addition, the inclusion of more articles and the relaxation of the control of article quality may some limitations of this study.

Further studies are needed to evaluate the effects of epidural analgesia on maternal and infant outcomes, especially long-term neurobehavioral effects on neonates.

AUTHOR CONTRIBUTIONS

Xue Bai and Dandan Zhang designed the study and drafted the manuscript; Yuxiao Wan searched strategy; Zhiqiang Feng and Donghai Yu designed the statistical analysis plan; Dandan Zhang reviewed the manuscript. All authors take responsibility for appropriate content.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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