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The effect of incubator humidity on morbidity and mortality in preterm infants: a systematic review

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Abstract

Purpose To assess the association between different incubator humidity levels and clinical outcomes in preterm infants.

Background Since there is no well-accepted standard for delivery of incubator humidity for preterm infants. A meta-analysis is needed to summarize the status of current research.

Methods Databases searched included PubMed, MEDLINE, the Cochrane Library, Embase, Ovid, Google scholar and Web of Science, published between January 2000 and December 2023. Randomized control trials, prospective cohort studies and retrospective cohort studies were included if they assessed how different incubator humidity levels affected preterm infants with a gestational age < 34 weeks, published in English. Infection rates, the incidence of bronchopulmonary dysplasia and predischarge mortality were evaluated.

Results Included in this review were 3 randomized control trials and 3 cohort studies including 801 preterm infants. Findings revealed that a high humidity level increased the incidence of infection in preterm infants (*RR* = 1.26, 95% *CI* 1.02, 1.55, P = 0.03). No significant difference was found between a high incubator humidity level and the incidence of bronchopulmonary dysplasia or infant mortality.

Conclusions This study found that high humidity levels had a significant impact on the incidence of infection. Current evidence is limited by signifcant heterogeneity across studies, lack of data related to regarding the effects of factors such as humidity duration and humidity adjustment schemes on the outcomes.

Keywords Preterm infants, Incubator humidity, Morbidity, Mortality, Meta-analysis

Introduction

Approximately 15 million preterm infants are born every year worldwide, and this number is increasing annually [1]. Due to the immature development of various organs, preterm infants are more vulnerable to serious diseases while hospitalized, including bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), and other complications. Severe illness in preterm infants may even result in permanent disability or death [2–5]. Improving the clinical care of preterm infants and reducing the risk of serious

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complications are urgent issues in perinatal medicine that will enhance survival.

There is consensus among healthcare professionals that humidification is advantageous in the treatment of many preterm infants [6–8]. Compared with term infants and late preterm, preterm infants have immature skin development and incomplete function.High transepidermal water loss (TEWL) through their thin skin layers results in large amounts of body fluid being lost through non-dominant water loss, leading to dehydration, hypernatremia, and weight loss [9, 10]. Previous studies have shown that TEWL is inversely correlated with ambient relative humidity [11]. By increasing incubator humidity in the early stages after birth, the daily fluid requirements of preterm infants can be reduced [10]. However, increased incubator humidity level also has side effects. Ambient humidity may slow the development of the skin barrier [12], and persistently high humidity may accelerate microbial growth and reproduction, putting preterm infants at higher risk for developing infections [13, 14].

Current clinical practices involve varying levels of humidity. Neonatal intensive care units (NICUs) use a wide range of incubator humidity levels and durations [15]. In a survey of NICUs in France, Australia and New Zealand, the humidity levels ranged from 60 to 100% [16]. In a cross-sectional investigation involving Australia, Canada, the Czech Republic, India, and the United States, it was found that while all of the institutions surveyed had established guidelines for humidification in the NICU, the humidity settings varied considerably, both within institutions and between institutions and nations [6]. Glass and Valdez used the Johns Hopkins levels and quality of evidence framework to assign a specific level and quality code to each article on all aspects of patient outcomes related to incubator humidity [8]. Through a systematic review Glass et al. indicated that a relative humidity of 60%—70% is suggested in the first week after birth for preterm infants with a gestational age > 26 weeks. [8] Kao, Chen and Lien selected studies for integrated synthesis [7]. Through a systematic review Kao et al. indicated that for preterm infants with a gestational age ≤ 30 weeks or a weight ≤ 1000 g, the relative humidity should be 70%—80% in the first week after birth and 50%—60% in the second week, and the duration should not exceed two weeks. [7] However, neither systematic review performed a meta-analysis [7, 8]. A meta-analysis consolidates sample sizes to increase the potential of testing power by synthesizing the results of multiple small study samples where the data have similar characteristics. Thus, the meta-analysis method was applied to the current studies within our systematic review, to evaluate the impact of high incubator humidity levels on the incidence of morbidity and mortality in preterm infants.

Methods

The review was registered with PROSPERO. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines (PROSPERO: CRD42023401195).

Study selection criteria

The inclusion criteria were as follows: (1) Preterm infants born at gestational age < 34 weeks. (2) Assess the use of different levels of incubator humidity. (3) Study types included were Randomized control trials (RCTs), prospective cohort studies, and retrospective cohort studies. (4) Primary outcomes assessed were mortality and morbidity related to infection and BPD. Studies with missing data, studies for which data could not be extracted and studies published in languages other than English were not included.

In our initial examination of the literature, we found that there were few high-quality RCTs related to our research question and of those we found most had very small sample sizes. As such we decide to included cohort studies in our sample to increase the overall sample size. The range of high humidity levels is obscure. The Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN) suggested that infants with extremely low birth weight should be kept in an incubator with an ambient humidity level that ranges from 70 to 85%, depending on gestational age [17]. For Glass and Valdez, it was suggested that the incubator humidity level should not exceed 70% when preterm infants develop a skin barrier in the first days of life and do not require humidity protection to minimize evaporative heat loss [8]. NICU thermal environment standards specify 22–26 °C (72–76°F) as an acceptable range for air temperature and 30–60% relative humidity [18].Considering that the humidification level of most incubators starts at 70%, the initial humidity setting of the incubator was ≥ 70% in this study, which is regarded as a relatively high humidity level for this research. Other interventions included an initial incubator humidity level of < 70% or no extra humidification.

The primary outcome measures were infection rates, the incidence of BPD and infant mortality. For review, infection rates were defined as the presence of urine, blood or cerebrospinal fluid infections.According to the criteria of the National Institute of Child Health and Human Development (NICHD) in 2001, any premature infant with oxygen dependence (oxygen concentration > 21%) for more than 28 days was classified as having BPD. We used this same criteria for this review. Mortality

was limited to include only predischarge mortality for this review.

Literature searches and data extraction

Several databases were searched, including PubMed, MEDLINE, the Cochrane Library, Embase, Ovid, Google scholar and Web of Science. Because the preliminary search showed that associated literature from the twentieth century was limited, literature was searched between January 2000 and December 2023 to ensure that the research findings precisely reflected current clinical practice.A combination of subject terms, free words, and Boolean logical operators was adopted for the search strategy.A manual search of relevant references was manually retrieved.

The search terms were infant*/Preterm/Premature/Prematurity/Neonatal/ "VLBW"/ "ELBW".

/incubator/Radiant Warmers/humidification/humid*/humidity. Two researchers reviewed the titles and abstracts and then selected which works should be included based on the inclusion and exclusion criteria. When the opinions of the two researchers differed, a third researcher with greater qualifications arbitrated the matter until consensus. The extracted data included basic data (author, year of publication, baseline situation), sample sizes, intervention measures, outcome indicators, etc.

Risk of bias assessment and evidence evaluation

RCTs were evaluated using the Cochrane Collaboration Network risk of bias assessment criteria [19]. The Cochrane Risk of Bias 1(ROB 1) was used for RCT. Two researchers independently assessed literature quality in a double-blind manner. The following were evaluated: random sequence generation, allocation concealment, the blinding of subjects and implementors, the blinding of outcome assessors, the integrity of outcome data, selective reporting of findings, and other sources of bias. On an article-by-article basis, each included study was assessed as having a "low risk of bias", a "high risk of bias" or an "unclear" risk of bias.The quality of the literature was divided into 3 levels: Grade A: Low bias and meeting all of the above criteria; Grade B: Moderate bias and meeting some of the above criteria; and Grade C: High risk of bias and not meeting any of the above criteria; submissions classified as Grade C were excluded. After the completion of independent assessments, the two researchers discussed and reached a consensus on the assessment results, and if there was a disagreement, a third researcher was consulted.

The Newcastle–Ottawa Scale (NOS) was used to evaluate the bias risk of cohort studies [20].The NOS includes 4 items for subject selection (4 points), 1 item for comparability between groups (2 points) and 3 items for outcome measurement (3 points), for a total score of 9 points. Research quality was divided into high-quality research (final score ≥ 6), medium-quality research (final score $= 5$), and low-quality research (final score < 5). Only medium- and high-quality documents with a score of 5–9 were included in this study.

The GRADE approach was used to assess evidence quality and recommendations [21]. Evidence quality is divided into four categories by the GRADE approach: high, moderate, low, and very low. Observational studies receive a low grade, while randomized controlled trials receive a high rating. When the publication link has serious problems, the level of evidence decreases. The GRADE approach classifies downgrading reasons into five categories: risk of bias, inconsistency, indirectness, imprecision, and publication bias. Observational studies with large effect sizes, defined as an $RR \leq 0.5$, are upgraded.

Data analysis

Review Manager 5.4 was used for the completion of the metanalysis. Firstly, a quantitative synthesis analysis was conducted of all included studies, and then a second stratified analysis was conducted by study type (RCT or cohort study). For enumeration data, the relative risk (RR) and its 95% confidence interval (95% CI) were used to determine the effect size. Included studies were subjected to the heterogeneity test, and the fixed effect model was used with no statistical heterogeneity ($P > 0.1$, $I^2 \leq 50\%$); the random effect model was used for studies with statistical heterogeneity ($P \leq 0.1$, $I^2 > 50\%$). The combined effect size was used for hypothesis tests, and $P < 0.05$ indicated that the outcomes were statistically significant. STATA version 14 software (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP) was used to execute the sensitivity analysis and publication bias test (Egger test).

Results

The literature search and screening process is shown in Fig. 1. A total of 801 subjects were included in 6 studies, including 3 randomized controlled trials ($n = 246$) and 3 cohort studies ($n = 555$).

The demographics of the population included studies are listed in Table 1. The Cochrane Collaboration Risk of Bias Assessment Criteria were used to assess the risk of bias for the included RCTs. All three of the included randomized controlled trials received a grade of B for literature quality. Figures 2a and b display the methodological quality assessment of the included studies. The three included cohort studies were evaluated for risk of bias using the NOS. According to the NOS, the three studies were relatively complete regarding the clarity

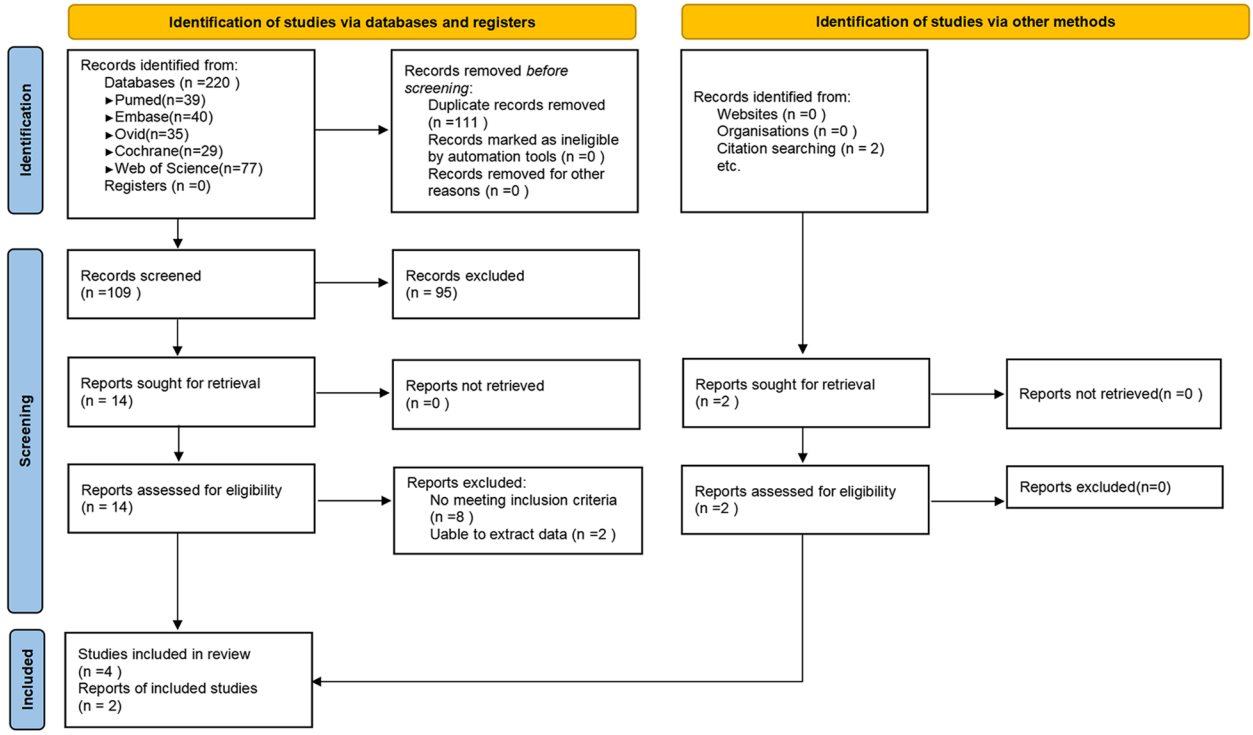


Fig. 1 PRISMA Flow diagram of studies selection

of cohort study comparability and follow-up time, and they all received an NOS score ≥ 6, indicating high quality. Table 2 displays the information mentioned above. As shown in supplemental Table 1, GRADE was used to evaluate the quality of the evidence.

Results of the meta-analysis

The effect of a high humidity level on infection

Overall, five studies [10, 22–24, 26] ($n=583$) compared the effect of a high humidity level on the incidence of infection in preterm infants. Utilizing the fixed effect model, the outcomes showed no heterogeneity among the studies when the effects of the included literature were combined. The meta-analysis results showed that a high humidity level increased the incidence of infection in preterm infants ($RR=1.26$, 95% CI 1.02, 1.55, $P=0.03$). The incidence of infection was 1.26 times higher in the group with a high humidity level than in the group with a low humidity level (Fig. 3a).

Of the 5 studies considered above, three were RCTs ($n=246$) which compared the effect of a high humidity level on infection rates in premature infants. The findings of the meta-analysis revealed that using a high humidity level may increase the incidence of infection in preterm infants ($RR=1.47$, 95% CI 1.01, 2.14, $P=0.04$), which was 1.47 times higher in the group with a high humidity level than in the group with a low humidity level.

Also included above, two cohort studies ($n=337$) compared the effect of a high humidity level on infection rates in premature infants. According to the meta-analysis findings, there were no significant differences between the groups with high and low humidity levels ($RR=1.16$, 95% CI 0.91, 1.5, $P=0.23$).

The effect of a high humidity level on the incidence of BPD

Four studies [10, 23, 24, 26] ($n=417$) compared the effect of a high humidity level on the incidence of BPD in preterm infants. The combined effects of the included literature revealed no evidence of study heterogeneity ($P=0.29$, $I^2=19\%$), and thus we used the fixed effect model. The results revealed that there was no significant difference between the groups with high and low humidity levels ($RR=1.07$, 95% CI 0.86, 1.33, $P=0.53$) (Fig. 3b).

Of the four studies included above, two RCTs [23, 24] ($n=110$) compared the effect of a high humidity level on the incidence of BPD in preterm infants. According to the meta-analysis findings, using a high humidity level may put preterm infants at greater risk of BPD ($RR=1.7$, 95% CI1.01, 2.86, P = 0.05). Within the two cohort trials, also included above [10, 26], ($n=307$) each compared the effect of a high humidity level on the incidence of BPD in preterm infants. The results revealed that there was no significant difference between the groups with high and

Table 1 Characteristics of included studies in systematic review

Author year	Country	Study type	Sample size (n)		Sample Characteristics (GA,wk/BW,g)		Humidity levels (%)		Duration of humidity (day)		Outcomes
			experimental	control	experimental	control	experimental	control	experimental	control	
Helder 2008 [22]	Netherlands	RCT	65	71	24-30w		80	70	14	14	Infection Mortality
Meyer 2001 [23]	New Zealand	RCT	30	30	< 33w BW < 1750 g		70–80	None	3/5	0	Infection BPD Mortality
Kong 2011 [24]	Australia	RCT	25	25	≤ 28 w BW500-1300 g		80	70	12.7 ± 0.6[a]	12.4 ± 1.3[a]	Infection BPD
Sung 2013 [25]	Korea	Cohort	121	97	22-24w BW < 1000 g	> 26w BW < 1000 g	95	60	7	7	Mortality
Gaylord 2001 [26]	America	Cohort	85	70	< 30w BW < 1000 g		70	None	No clear	0	Infection BPD Mortality
Kim 2010 [10]	America	Cohort	95	87	< 30w BW < 1000 g		70–80	None	25.5 ± 1.1[a]	0	Infection BPD Mortality

GA gestational age, *BW* birth weight

[a] Data presented as mean ± S

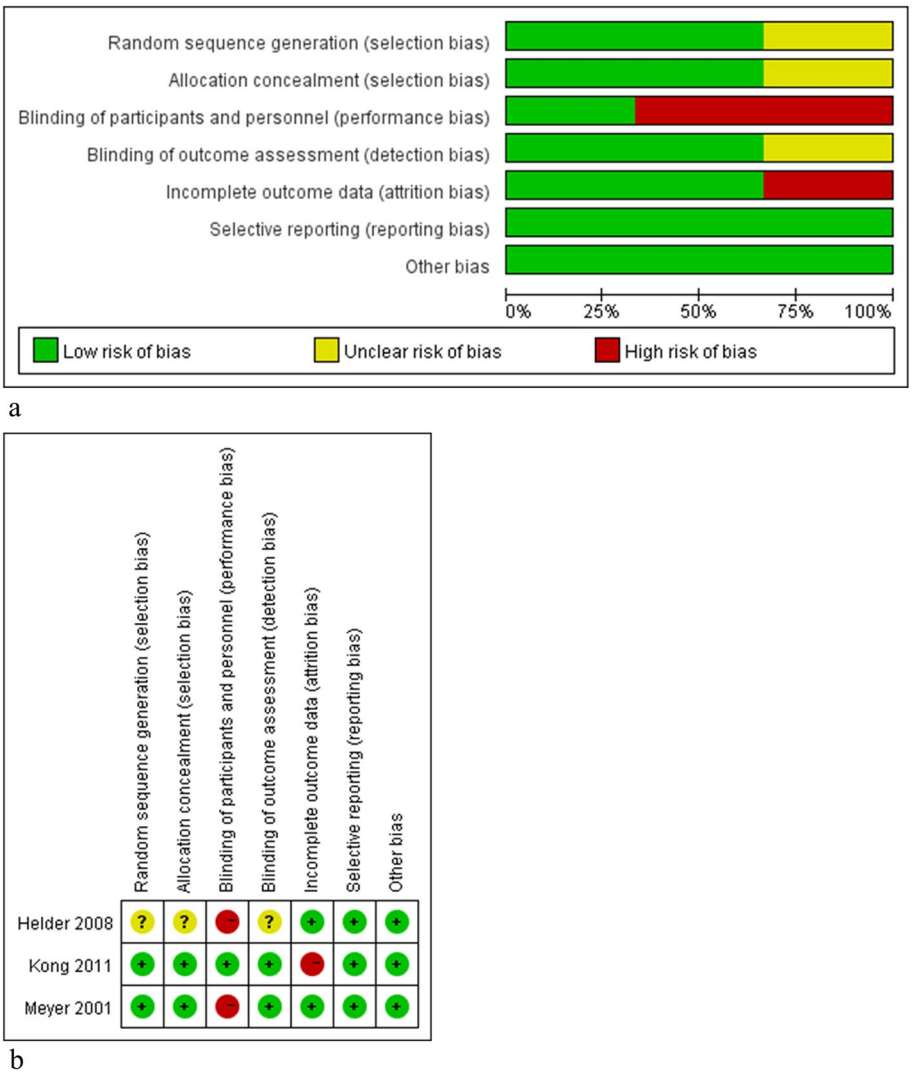


Fig. 2 a Risk of bias in the included trials. b Risk of bias in the included trials

Table 2 Cohort studies scored according to the the NOS scale

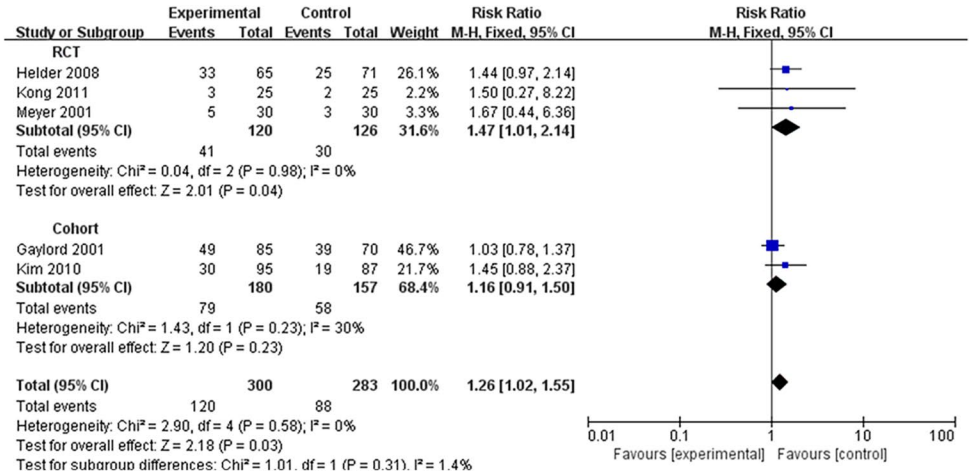
Study	Selection	Comparability	Outcome	Score
Gaylord 2001 [26]	4	1	2	7
Kim 2010 [10]	3	1	3	6
Sung 2013 [25]	3	1	3	7

low humidity levels within the cohort studies (*RR* = 0.97, 95% *CI* 0.76, 1.24, P = 0.82).

The effect of a high humidity level on mortality

Five studies [10, 22, 23, 25, 26] (*n* = 751) compared the effect of a high humidity level on the incidence of mortality predischarge in preterm infants. The combined effects of the included literature revealed no evidence of study heterogeneity (P = 0.14, I^2 = 42%) and thus we used the fixed effect model. The results revealed that there was no significant difference between the groups with high and low humidity levels (*RR* = 1.46, 95% *CI* 0.82, 2.6, *P* = 0.84) (Fig. 3c).

Of the above included studies, the two RCTs [22, 23] (*n* = 196) examined the effect of a high humidity level on mortality. The results revealed that there was no significant difference between the groups with high and low levels of humidity (*RR* = 1.32, 95% *CI* 0.1, 17.66, P = 0.84). However, in the three cohort studies [10, 25, 26] comparing the effect of a high humidity level on mortality, the results revealed that a high humidity level significantly increased the mortality rate of preterm infants, which was 1.73 times higher in infants with a high humidity level than in infants with a low humidity level (RR = 1.73, 95% CI 1.17, 2.57, *P* = 0.006).



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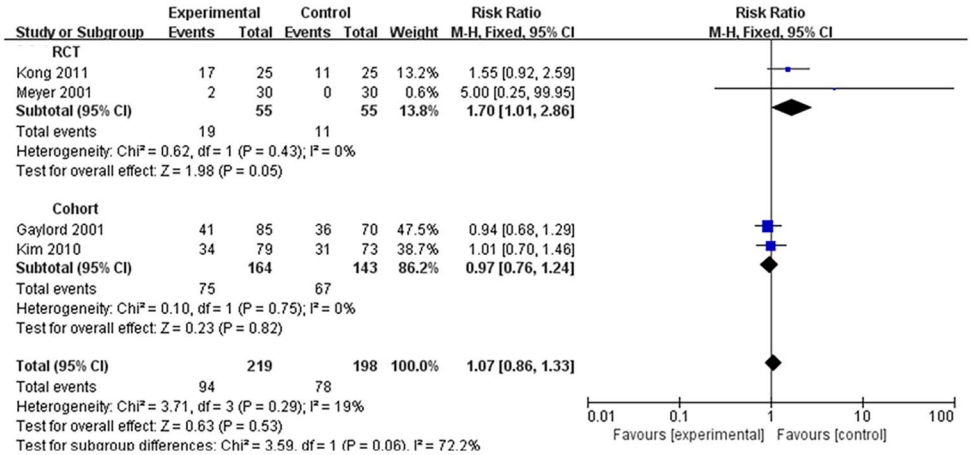

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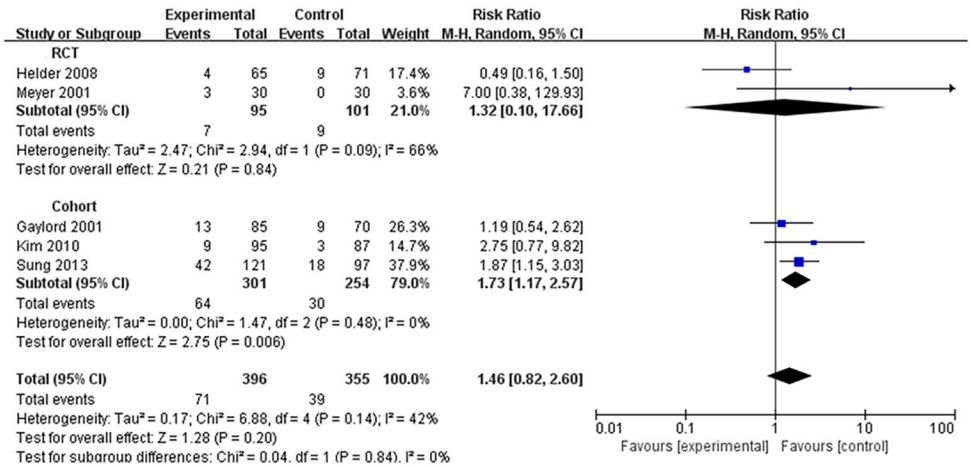

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Fig. 3 Forest plot. **a** The effect of high humidity environments on the incidence of infection. **b** The effect of high humidity environments on the incidence of BPD. **c** The effect of high humidity environments on mortality

Sensitivity analysis

To eliminate the impact of different incubators on the results for infection risk, a sensitivity analysis was conducted to determine whether the results were stable. Five studies [10, 22–25] used double-walled incubators, whereas Gaylord et al [26] used single-walled incubators. After sensitivity analysis, as shown in Figs. 4a,b and c, no significant effects on heterogeneity were demonstrated across studies.

Publication bias

The results of the Egger test revealed that the infection rate ($P=0.286>0.05$), BPD incidence rate ($P=0.208>0.05$), and mortality rates ($P=0.993>0.05$) were all unaffected by publication bias.

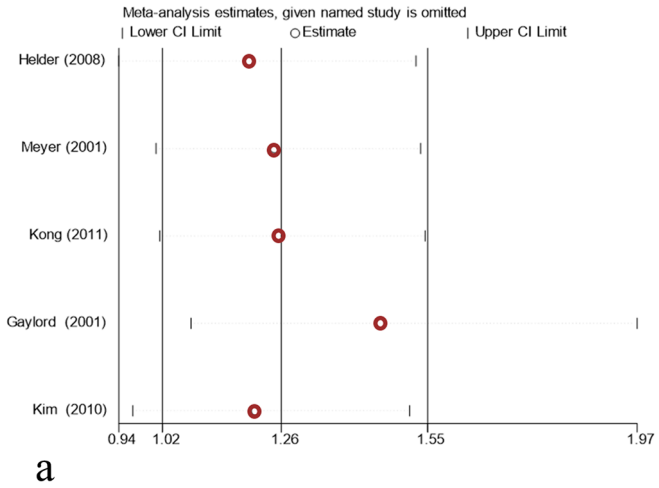
Discussion

This systematic review aimed to investigate the effect of incubator humidity levels on morbidity and mortality in preterm infants. It should be the first review that have attempted to conduct a meta-analysis to summarize the current research status. Quantitative synthesis analysis of all included studies was conducted, and stratified by study design, and then the stability of the results.

According to the meta-analysis of the studies that were included, there was a significant increase in the risk of infection in preterm infants when the incubator humidity level was high, and this result was particularly evident in RCTs (quality of evidence: low). This result was consistent with the research of Lynam [13] and Etienne [14]. Continuously high humidity can lead to faster growth and reproduction of microorganisms, which increases the risk of sepsis in preterm infants because humidity increases condensation inside the incubator [13, 14]. Due to the impact of high heat and humidity on the relatively colder inner wall of the incubator, more condensation may be produced. Prazad [27] found that volatile organic compound concentrations in the air increased when the humidity in the chamber was raised to 50%. When the average temperature and relative humidity of the incubator were set too high, the level of microbial contamination increased significantly. Pritik [28] noticed that the diversity of skin fungi was higher in environments with higher humidity when monitoring the skin flora of extremely preterm infants, indicating that humidity is closely related to the reproduction and growth of fungi. According to previous studies, mold grows in conditions with at least 70% humidity, while yeast and gram-positive and gram-negative bacteria grow in environments with 80% to 95% humidity [29].

However, the design of humidification systems in modern incubators has changed over time to decrease the risk of infection [30]. Double-walled incubators reduce condensation and incorporate hot-water equipment, which kills most organisms and keeps bacteria out of the air [13]. Significantly, there is still a risk of external microorganisms being introduced into this warm, moist environment by caregivers' hands. To eliminate the impact of different incubators on the results for infection risk, a sensitivity analysis was conducted to determine whether the results were stable. Five studies [10, 22–25] used double-walled incubators, whereas Gaylord et al [26] used single-walled incubators. Figure 4 shows that excluding the study by Gaylord et al [26] did not affect the results. It is unclear whether the incubators used in the studies provided sterile humidity. Due to the studies being published between 2001 and 2013, further trials are needed to verify whether the conclusions of this article that high humidity levels may increase infection rates apply to modern incubators.

Additional factors to examine, studies showed that the gestational age of the included subjects may affect the findings [11, 29]. Preterm infants with a lower gestational age need to be cared for in an incubator environment with a longer duration and higher initial humidity level, which may affect the incidence of infection. The maturity of skin barrier function in preterm infants depends on their gestational age. Regarding skin development, the epidermis matures gradually in the last quarter of pregnancy [11]. Preterm infants born at a younger gestational age have less developed skin. The immaturity of skin barrier function in preterm infants is mainly related to the development of the stratum corneum. The stratum corneum, one of the skin structures, dissipates heat through evaporation, controls transepidermal water loss, and protects the body from pathogens and toxins. At approximately 24 weeks of gestation, stratum corneum development begins.Extremely low-birth-weight infants with a gestational age of less than 24 weeks barely have stratum corneum, and premature infants born at less than 30 weeks gestation have only two to three stratum corneum layers [12].There is evidence that by 30 to 32 weeks of gestational age, the stratum corneum has almost fully developed [31].The AWHONN guideline mentioned that the length of time it takes for skin to mature usually takes one week for preterm infants born at 25–29 weeks, 2–3 weeks for preterm born at 24 weeks and less. But small for gestational age infants' skin matures much faster than other babies [17]. Additionally, preterm infants need incubators with high initial humidity levels for extended periods, which may affect the incidence of infection. However, in the current research on the effect of incubator humidity on preterm infants, the gestational age of the included subjects was quite different, suggesting that future studies should be stratified based on gestational age. Notably, the following precautions might decrease



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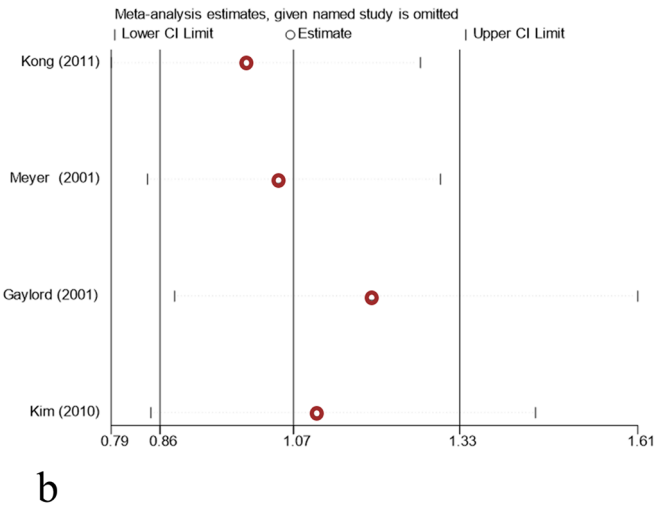

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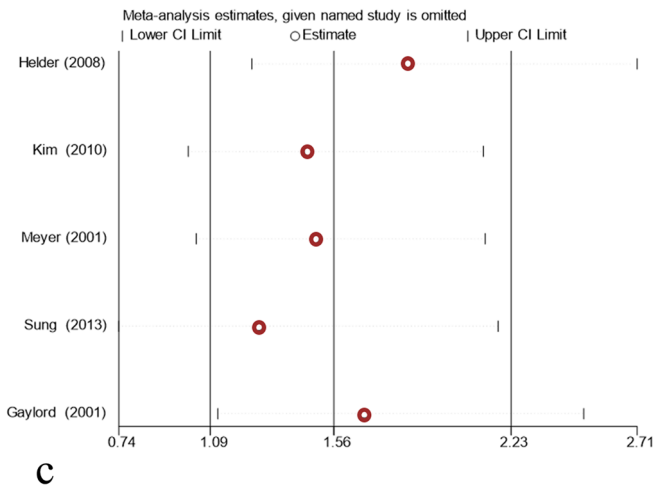

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Fig. 4 Sensitivity analysis. **a** The incidence of infection. **b** The incidence of BPD. **c** The incidence of mortality

the risk of neonatal infections and even late sepsis when the incubator is set to a high humidity level: reducing the duration of a high humidity level, thoroughly cleaning the incubator, and replacing the sterile water daily [29, 32].

This study did not find that a high incubator humidity level had significant effect on either the incidence of BPD or the mortality rate of preterm infants (quality of evidence: low). This is consistent with Kao's research conclusion [7]. The principle of providing humidity is based on thermal regulation and reducing heat loss due to evaporation. In a dry and cold environment, the rate of evaporation heat exchange between the skin surface and the ambient air can be very high [33]. Increasing the incubator humidity level in the early stages after birth can continuously reduce insensible water loss, reduce the daily fluid requirements of extremely preterm infants, improve water and electrolyte balance and maintain thermal stability, reducing mortality rates [10]. There is not yet sufficient evidence to confirm the direct impact of high incubator humidity levels on the incidence of BPD or the mortality rate of preterm infants. Further high-quality RCTs will be required to verify the outcome.

However, the findings obtained for the two research types—RCTs and cohort studies—were distinct in this study after conducting stratified analysis. The subgroup analysis of RCTs showed higher risk of BPD and the cohort studies showed a higher mortality rate. There are two possible reasons for this difference: first, the sample size of the included RCTs was far smaller than that of the included cohort studies, which could explain the discrepancy. Three RCTs ($n=246$) and three cohort studies ($n=555$) were included in this study. Second, the baselines of two RCTs [23, 24] and three cohort studies [10, 25, 26]were unbalanced. According to the assessment of included studies' quality of evidence, the combined effect size of the two RCTs was large (RR = 1.7) when analyzing how different humidity levels impacted the incidence of BPD in preterm infants. However, the sample size of this experimental group ($n=55$) and control group ($n=55$) was insufficient to meet the optimal information size standard, so the grade was downgraded by one level due to severe inaccuracy. When examining the effect of various humidity levels on the mortality of preterm infants, two RCTs were combined to achieve an I [2] of 66%, and the high heterogeneity produced severe inconsistency, so the grade was downgraded by one level. As some control groups were in a non-humidified environment and some were in a humidified environment, two RCTs and three cohorts were both downgraded by one level having serious indirectness. Even so, the heterogeneity between RCTs and cohort studies was not significant, less than 50%. This means that there may be some confounding factors in the different research designs that affect the results, and more research is needed to guide practice recommendations. Overall, merging all the studies yielded more reliable results. Therefore, the combined results from cohort studies and RCTs may represent the true situation rather than RCTs or cohort studies alone.

Implications for practice

Evidence has demonstrated that when the initial incubator humidity level is high—at more than 70%— the incidence of infection in preterm infants is significantly increased. When creating a humidity delivery plan for preterm infants, the impact of high humidity levels on the infection rate of preterm infants should be carefully considered. To reduce the risk of infection in preterm infants, we can implement incubator disinfection and reduce the duration of a high humidity level when making a plan for humidity management.

Implications for research

More large clinical trials and humidity-related research including preterm infants of differing gestational ages particularly those from younger gestational ages must be conducted in the future.

Limitations of this study

To ensure the credibility of results and reduce the risk of bias in the review, we only included studies that meet our selection criteria rather than increased the number of studies. So it cannot be denied that the number of studies included in this review is less than Glass et al. review [8]. The search revealed that the number of pertinent experimental studies in the field, particularly RCTs, was small. The quality of evidence were low, the risk benefit could not be decided, which can not accurately guide clinical practice. The humidity levels in the control group of existing research designs varied significantly because there are no correlative standards regarding humidity for the care of preterm infants. Although still acceptable, the heterogeneity of the study designs may have led to smaller effect sizes. Due to the lack of data regarding the effects of factors such as humidity duration and humidity adjustment schemes on the outcomes, subgroup analysis on gestational age and birth weight was not conducted. The findings of this review may not be applicable to infants who are extremely preterm or very preterm neonates.

Conclusions

This review summarized the available evidence relating to the effect of humidity levels on complications and mortality in preterm infants. This study found that high humidity levels had a significant impact on the incidence of infection but had no impact on mortality or the incidence of bronchopulmonary dysplasia. However, the evidence is limited by signifcant heterogeneity across studies, lack of data related to regarding the effects of factors such as humidity duration and humidity adjustment schemes on the outcomes.

Other information

The article was registered with PROSPERO. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines. Different from the protocol, the outcome indicators that were not presented were the incidence of hypernatremia, intravascular hemolysis and patent ductus arteriosus. During the search process, it was found that few studies observed and described these indicators, resulting in the inability to conduct a meta-analysis [PROSPERO: CRD42023401195].

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Abbreviations

NICUs	Neonatal Intensive Care Units
BPD	Bronchopulmonary dysplasia
IVH	Intraventricular hemorrhage
PVL	Periventricular leukomalacia
TEWL	Transepidermal water loss
RCTs	Randomized controlled trials

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12887-025-05538-3.

Supplementary Material 1.

Supplementary Material 2

Supplementary Material 3

Acknowledgements

Not Applicable

Authors' contributions

Z.C. designed the study, collected, and analyzed data, drafted the initial manuscript, and reviewed and revised the manuscript; R.L. collected and analyzed data, reviewed, and revised the manuscript; H.W. reviewed and revised the manuscript; B.S. and Q.C. made supportive contributions and contributed to the critical revision of the manuscript.All authors have read and approved the manuscript.

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Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

Not Applicable.

Consent for publication

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