

Effect of Endotracheal Suctioning on Infants Born through Meconium-Stained Amniotic Fluid: A Meta-analysis

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Abstract

Objective Meconium is a common finding in amniotic fluid and placental specimens, particularly in term and post-term pregnancies. The objective of this paper was to perform a meta-analysis to examine the impact of endotracheal suctioning on the occurrence of meconium aspiration syndrome (MAS), mortality, and complications.

Study Design PubMed, EMBASE, and the Cochrane library were systematically searched for comparative studies. Odds ratios (ORs), weighted mean differences (WMDs), and corresponding 95% confidence intervals (CIs) were used to compare the outcomes.

Results Twelve studies were included in the meta-analysis. There were no significant impacts of endotracheal suctioning on the occurrence of MAS (OR = 3.05, 95% CI: 0.48–19.56), mortality (OR = 1.25, 95% CI: 0.35–4.44), the need for mechanical ventilation (OR = 4.20, 95% CI: 0.32–54.72), the occurrence of pneumothorax (OR = 0.99, 95% CI: 0.34–2.85), persistent pulmonary hypertension of the newborn (PPHN), (OR = 1.31, 95% CI: 0.58–2.98), hypoxic-ischemic encephalopathy (HIE) (OR = 0.82, 95% CI: 0.52–1.30), and length of stay (WMD = −0.11, 95% CI: −0.99–0.77).

Conclusion Routine endotracheal suctioning at birth is not useful in preventing MAS, mortality, mechanical ventilation, PPHN, HIE, and prolonged length of stay in neonates born through MSAF.

Keywords

- ▶ meconium aspiration syndrome
- ▶ suction
- ▶ odds ratios
- ▶ endotracheal
- ▶ meta-analysis

Key Points

- Routine suctioning is not recommended for newborns.
- Endotracheal aspiration is not beneficial for MAS.
- Future research may focus on selected neonates.

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Meconium is a common finding in amniotic fluid and placental specimens, particularly in term and post-term pregnancies.¹⁻⁴ The most important consequence of meconium-stained amniotic fluid (MSAF) is the meconium aspiration syndrome (MAS).^{1-3,5} The MAS is a condition marked by respiratory distress in a neonate after delivery through MSAF.^{1-3,5} The aspiration of meconium usually occurs in utero but may also happen after delivery.^{1-3,5} Factors that increase the possibility of MAS include intra-uterine growth restriction, delivery at >41 weeks of gestation, heavy MSAF, the presence of meconium below the vocal cords, and fetal heart rate abnormalities during labor.^{2,3,6,7} Symptoms of MAS usually develop within 15 minutes of birth but may take up to 12 hours. Neonates usually present with respiratory distress, including tachypnea, cyanosis, grunting, nasal flaring, and retractions.¹⁻³ If fetal distress is present, neonates may also have symptoms of neonatal depression, including bradycardia, decreased respiratory effort, and reduced muscle tone.¹⁻³ At least 5% of infants born through MSAF develop MAS.^{1-3,5,8,9} MAS continues to be a threat to many newborns throughout the world, with a fatality rate of 5 to 40%, in addition to short- and long-term pulmonary and neurological developmental sequelae.^{2,3,5,10}

Universal intrapartum suction of infants with MSAF and postnatal suction of vigorous infants have been used in an attempt to decrease the incidence and severity of MAS by clearing the airway, but the practice of endotracheal suctioning of meconium-stained non-vigorous newborns has been questioned due to procedure-related harms and uncertain benefits. The current guidelines from the American College of Obstetricians and Gynecologists (ACOG) do not recommend the routine intrapartum suctioning of all newborns with MSAF; gentle suctioning can be done in vigorous neonates, and suctioning is not recommended for non-vigorous newborns, but endotracheal suctioning can be considered if breathing is obstructed by a meconium plug.¹¹⁻¹³ Nevertheless, available studies report conflicting results with studies supporting endotracheal suctioning,^{14,15} supporting no endotracheal suctioning,^{16,17} and with negative results.^{7,18-22} When this meta-analysis was conducted, there was no meta-analysis on the topic. Still, one meta-analysis was published in the meantime, suggesting no benefit of endotracheal suctioning in non-vigorous newborns.²³

Therefore, we performed a meta-analysis and systemic review to examine the impact of endotracheal suctioning on MAS occurrence, mortality, and complications in all infants born through MSAF. The results could shed some light on the possible benefits of this practice.

Materials and Methods

Literature Search

This systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines²⁴ and the PICO methodology.²⁵ PubMed, EMBASE, and the Cochrane library

were systematically searched for studies published up to November 2019. The search strategies are presented in **Supplemental Table 1** (available in the online version).

The eligibility criteria were as follows: (1) population: newborn infants born through MSAF; (2) intervention: endotracheal suctioning; (3) control: without endotracheal suctioning; (4) study types: cohort study and randomized control trial (RCT); and (5) language: limited to English.

Search Strategy

We performed a systematic search from the PubMed, Embase, and Cochrane library databases for available papers published up to November 2019 using the Mesh terms "MAS," and "Suction," as well as relevant keywords. The reference lists of the identified papers were reviewed to find additional eligible studies.

Data Extraction and Quality Assessment

The selection and inclusion of studies were performed in two stages by two independent reviewers (Q.W. and Q.L.). This included the analysis of the titles and abstracts, followed by the full texts. Disagreements were resolved by discussion with a third reviewer (W.C.).

Data including authors, publication year, study design, gestational maturity, birth weight, vigorous/non-vigorous babies, MAS, mortality, pneumothorax, persistent pulmonary hypertension of the newborn (PPHN), mechanical ventilation, and hypoxic-ischemic encephalopathy (HIE) were extracted from the papers.

The RCTs were evaluated according to the Cochrane risk bias tool.²⁶ The observational studies were evaluated according to the Newcastle-Ottawa Scale (NOS).²⁷

Statistical Analysis

All analyses were performed using the STATA SE 14.0 software (StataCorp, College Station, TX, USA). Odds ratios (ORs), weighted mean differences (WMDs), and the corresponding 95% confidence intervals (CIs) were used to compare the outcomes. Statistical heterogeneity among the included studies was calculated using Cochran's Q-test and the I^2 index ($I^2 > 50\%$ indicated high heterogeneity). The random-effects model was used when high heterogeneity was present among studies; otherwise, the fixed-effects model was applied. p -Values < 0.05 were considered statistically significant. Potential publication bias was assessed using funnel plots and Egger's and Begg tests.²⁶

Results

Literature Search

The database search identified 479 records, and 318 records were left after removing the duplicates. After screening the titles and abstracts, 55 full-text articles were assessed for eligibility. Finally, 12 articles were included in the meta-analysis (**Supplemental Fig. 1** and **Supplemental Table 1**, available in the online version). **Supplemental Table 2** (available in the online version) summarizes the included papers published between 1975 and 2019. There were seven

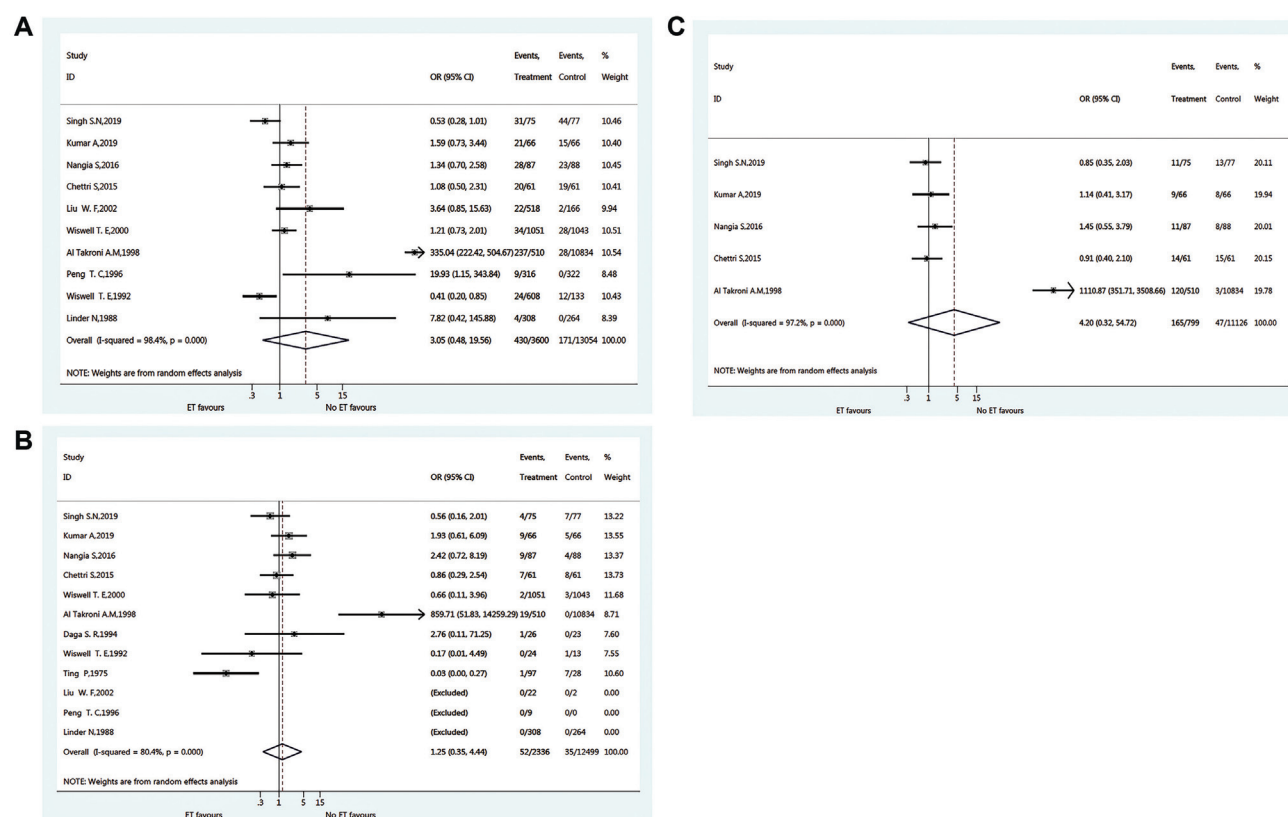


Fig. 1 (A) Forest plot of MAS. (B) Forest plot of mortality. (C) Forest plot of mechanical ventilation.

RCTs and five cohort studies. The sample sizes ranged from 122 to 11,344 neonates, for a total of 16,828. **Supplemental Table 2** (available in the online version) presents the bias analysis of the RCTs; except for the RCT by Singh et al,¹⁴ all other RCTs^{18–22,28} had low probabilities of biases. **Supplemental Tables 3–4** (available in the online version) present the NOS evaluation of the cohort studies. Among the cohort studies, three^{16,17,29} scored seven stars on the NOS, while two^{7,15} scored eight stars.

MAS

Ten studies^{7,14–22} could be included in the MAS analysis. The meta-analysis showed no significant impact of endotracheal suctioning on the occurrence of MAS (OR = 3.05, 95% CI: 0.48–19.56, $p = 0.239$) (**Fig. 1A**). Heterogeneity was observed, and the random-effect model was used ($I^2 = 98.4\%$, $p < 0.001$). The subgroup analyses showed similar results (all $p > 0.05$; **Table 1**). The sensitivity analysis indicated that the study by Al Takroni et al¹⁶ introduced heterogeneity

Table 1 Subgroup analysis of MAS

MAS	Treatment	Control					
	<i>n</i>	Event/total (%)	Event/total (%)	OR (95% CI)	<i>P</i>	<i>I</i> ²	<i>P</i> _{heterogeneity}
MAS in all	10	430/3,600 (11.9)	171/13,054 (1.3)	3.051 (0.476, 19.565)	0.239	98.4	<0.001
RCT	6	138/1,648 (8.4)	129/1,599 (8.1)	1.105 (0.751, 1.626)	0.611	38	0.153
Observational study	4	292/1,952 (15.0)	42/11,455 (0.4)	9.952 (0.115, 860.352)	0.313	99	<0.001
Aisa	5	337/799 (42.2)	129/11,126 (1.2)	3.347 (0.170, 65.949)	0.427	99.1	<0.001
America	5	93/2,801 (3.3)	42/1,928 (2.2)	1.767 (0.601, 5.196)	0.301	76	0.002
Non-vigorous	4	100/289 (34.6)	101/292 (34.6)	1.027 (0.625, 1.687)	0.916	49.5	0.114
Vigorous	4	69/2,193 (3.1)	30/1,795 (1.7)	3.116 (0.898, 10.814)	0.073	57.5	0.07
Unclear	2	261/1,118 (23.3)	40/10,967 (0.4)	3.051 (0.476, 19.565)	0.488	99.6	<0.001
After 2010	4	100/289 (34.6)	101/292 (34.6)	1.027 (0.625, 1.687)	0.916	49.5	0.114
Before 2010	6	330/3,311 (10.0)	70/12,762 (0.5)	6.618 (0.321, 136.427)	0.221	98.8	<0.001
Sample size <200	4	100/289 (34.6)	101/292 (34.6)	1.027 (0.625, 1.687)	0.916	49.5	0.114
Sample size >200	6	330/3,311 (10.0)	70/12,762 (0.5)	6.618 (0.321, 136.427)	0.221	98.8	<0.001

Abbreviations: CI, confidence interval; MAS, meconium aspiration syndrome; OR, odds ratio; RCT, randomized control trial.

Table 2 Subgroup analysis of mortality

Mortality	Treatment		Control		OR (95% CI)	<i>p</i>	<i>I</i> ²	<i>P</i> _{heterogeneity}
	<i>n</i>	Event/total (%)	Event/total (%)					
Mortality in all	12	52/2,336 (2.2)	35/12,499 (0.3)		1.254 (0.354, 4.442)	0.725	80.4	<0.001
RCT	7	32/1,674 (1.9)	27/1,622 (1.7)		1.190 (0.686, 2.062)	0.536	0	0.503
Observational study	5	20/662 (3.0)	8/10,877 (0.1)		1.630 (0.002, 1,237.168)	0.885	94.4	<0.001
Aisa	6	49/825 (5.9)	24/11,149 (0.2)		2.952 (0.695, 12.542)	0.142	82.1	<0.001
America	6	3/1,511 (0.2)	11/12,499 (0.1)		0.161 (0.021, 1.230)	0.078	56.5	0.1
Non-vigorous	5	30/315 (9.5)	24/315 (7.6)		1.265 (0.710, 2.254)	0.425	0	0.423
Vigorous	4	2/1,390 (0.1)	3/1,309 (0.2)		0.661 (0.110, 3.964)	0.65	–	–
Unclear	3	20/631 (3.2)	8/10,875 (0.1)		1.630 (0.002, 1,237.168)	0.725	94.4	<0.001
After 2010	4	29/289 (10.0)	24/292 (8.2)		1.233 (0.645, 2.357)	0.527	17.7	0.302
Before 2010	8	23/2,047 (1.1)	11/12,207 (0.1)		1.464 (0.046, 46.945)	0.829	89.3	<0.001
Sample size <200	6	31/412 (7.5)	31/343 (9.0)		0.826 (0.297, 2.302)	0.715	66	0.012
Sample size >200	6	21/1,924 (1.1)	4/12,156 (0.03)		4.576 (0.028, 748.847)	0.559	91.5	<0.001

Abbreviations: CI, confidence interval; OR, odds ratio; RCT, randomized control trial.

(► **Supplemental Fig. 2A**, available in the online version). After excluding that study, there was no significant impact of endotracheal suctioning on the occurrence of MAS (OR = 1.16, 95% CI: 0.71–1.88, *p* = 0.554) (► **Supplemental Fig. 2B**, available in the online version). Meta-regression showed that the publication year was not associated with the occurrence of MAS (*p* = 0.277; ► **Supplemental Fig. 2C**, available in the online version).

Mortality

Nine studies [14–16,18–21,25,26] were included in the mortality analysis. The meta-analysis showed no significant impact of endotracheal suctioning on mortality (OR = 1.25, 95% CI: 0.35–4.44, *p* = 0.725) (► **Fig. 1B**). Heterogeneity was observed, and the random-effect model was used (*I*² = 80.4%, *p* < 0.001). The subgroup analyses showed similar results (all *p* > 0.05; ► **Table 2**). The sensitivity analysis indicated that Al Takroni et al. [16] introduced heterogeneity (► **Supplemental Fig. 3A**, available in the online version). After excluding that study, there was no significant impact of endotracheal suctioning on mortality (OR = 0.75, 95% CI: 0.32–1.77, *p* = 0.513) (► **Supplemental Fig. 3B**, available in the online version).

Mechanical Ventilation

Five studies^{14,16,18,19,22} could be included in the analysis of mechanical ventilation. The meta-analysis showed no significant impact of endotracheal suctioning on the need for mechanical ventilation (OR = 4.20, 95% CI: 0.32–54.72, *p* = 0.273; ► **Fig. 1C**). Heterogeneity was observed, and the random-effect model was used (*I*² = 97.2%, *p* < 0.001). After excluding the study by Al Takroni et al [16], similar results were still observed (OR = 1.04, 95% CI: 0.66–1.64, *p* = 0.869) but without heterogeneity (*I*² = 0%).

Other Outcomes

► **Fig. 2A to D** show that endotracheal suctioning does not affect the occurrence of pneumothorax (OR = 0.99, 95% CI:

0.34–2.85, *p* = 0.979; *I*² = 0%, *p* = 0.872) [14,19,20,25], PPHN (OR = 1.31, 95% CI: 0.58–2.98, *p* = 0.513; *I*² = 0%, *p* = 0.598) [14,18,20], HIE (OR = 0.82, 95% CI: 0.52–1.30, *p* = 0.405; *I*² = 12.9%, *p* = 0.317) [14,19,25], and the length of stay (WMD = −0.11, 95% CI: −0.99–0.77; *I*² = 72.8%, *p* = 0.025) [14,18,19].

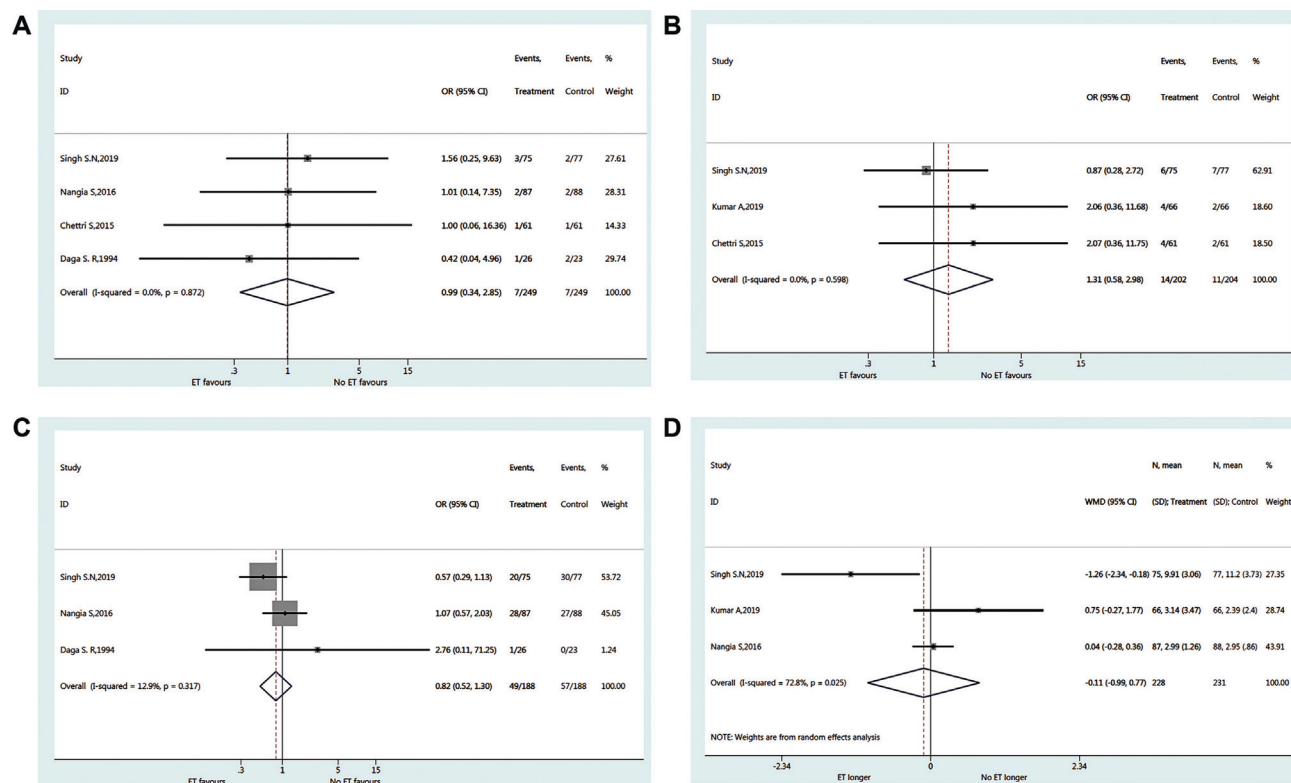
Publication Bias

The funnel plots revealed some publication bias regarding MAS (► **Supplemental Fig. 4A**, available in the online version) and mortality (► **Supplemental Fig. 4B**, available in the online version), but there were no significant differences in Egger's test (*P*_{MAS} = 0.348, *P*_{mortality} = 0.828) and Begg's test (*P*_{MAS} = 0.107, *P*_{mortality} = 0.754).

Discussion

Endotracheal suctioning of meconium-stained newborns has been questioned due to procedure-related harms and uncertain benefits.^{7,11–22} Therefore, the present meta-analysis aimed to examine the impact of endotracheal suctioning on MAS occurrence, mortality, and complications. The results strongly suggest that routine endotracheal suctioning at birth is not useful in preventing MAS, mortality, mechanical ventilation, PPHN, HIE, and prolonged length of stay in neonates born through MSAF.

In the present meta-analysis, Al Takroni et al¹⁶ systematically introduced significant heterogeneity in all analyses. This was a retrospective cohort study of 11,344 births at a hospital where the babies born through MSAF undergo intrapartum endotracheal suctioning, followed by intubation for asphyxiated babies and observation for vigorous ones. There was no distinction based on gestational age, while nine studies included term and post-term neonates, two studies did not mention the gestational age.^{7,15} Even though delivery through MSAF is more likely to occur in neonates at term or post-term,^{2,3,6,7} there is a possibility that the study by Al Takroni



et al¹⁶ included pre-term neonates. In addition, the incidence of delivery through MSAF was elevated, at 13.3%.

In the present meta-analysis of 16,828 newborns (12 studies), no benefit of endotracheal suctioning was observed in all newborns, irrespective of status. This is supported by a meta-analysis published while the present one was being conducted. In that recent meta-analysis of 581 newborns (four studies), endotracheal suctioning in non-vigorous newborns apparently did not improve neonatal outcomes.²³ Still, we used different inclusion criteria. Indeed, Phattrapayoon et al²³ included only four studies, while the present meta-analysis included 12. Using too stringent selection criteria carries the risk of decreasing the generalizability of the conclusions. The populations were different, with non-vigorous infants in Phattrapayoon et al²³ and infants born through MSAF in the present study. The outcomes were also different, the present meta-analysis examining MAS, mortality, the need for mechanical ventilation, the occurrence of pneumothorax, PPHN, HIE, and length of stay, while the previous meta-analysis examined MAS, pneumothorax, PPHN, secondary pneumonia, need for respiratory support, duration of mechanical ventilation, initial resuscitation, and others including shock, perinatal asphyxia, convulsions, neonatal mortality, blood culture-positive sepsis, and duration of hospital stay. Examining too many outcomes using a small number of studies increases the risk of misleading conclusions. In addition, because of the small number of studies included, subgroup analyses were very limited in Phattrapayoon et al.²³ Still, they reached a conclusion similar to the present meta-analysis. The meta-analysis by Phattrapayoon et al²³ demonstrated no benefits in non-

vigorous infants, while the present meta-analysis demonstrated no benefits in all infants born through MSAF.

The failure of endotracheal suctioning in improving the outcomes of the newborn might include the occurrence of meconium aspiration in utero, the migration of the meconium to the distant airways, and the impossibility of removing the meconium from those small airways.³⁰ In addition, even if some meconium could be aspirated from the distal airways, there is still a high possibility of some of them remaining plugged.¹⁸ In addition to the mechanical concept regarding the failure to aspirate the meconium, MAS induces pulmonary and systemic pathophysiological changes that include inactivation of surfactant,³¹ pulmonary hypertension,³² and activation of immunity,³³ which would lead to poor outcomes even if all meconium were removed. Therefore, the current guidelines from the ACOG do not recommend the routine intrapartum suctioning of all newborns with MSAF.¹¹ Instead, they recommend that gentle suctioning can be done in vigorous neonates but not in non-vigorous newborns and that endotracheal suctioning can be considered if breathing is obstructed by a meconium plug.¹¹ Those recommendations are supported by the American Heart Association (AHA)¹² and the 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science.¹³ Nevertheless, endotracheal suctioning might still be required in selected neonates. Indeed, despite that the changes in practice following Neonatal Resuscitation Program (NRP) have not increased the reported cases of MAS, an increase in neonatal intensive care unit admissions for respiratory distress has been observed, with higher rates of requirement for mechanical

ventilation, oxygen, and surfactants.³⁴ In addition, the main issue with endotracheal suctioning is the possible delay in the resuscitation of already compromised neonates with the possibility of asphyxia injuries.³⁵ The NRP guidelines state that positive pressure ventilation must be performed if required after endotracheal suction and evaluation.³⁶ Such forced ventilation might alleviate the impact of asphyxia despite a delay due to endotracheal suctioning. Therefore, future studies should focus on selecting the neonates who would benefit the most from endotracheal suctioning. Nevertheless, the most recent studies suggest no benefit, no harm either, of endotracheal suctioning.^{14,18,22} Nevertheless, those studies were performed in selected populations. Kumar et al¹⁸ and Singh et al¹⁴ showed that endotracheal suctioning did not prevent MSAF in non-vigorous neonates of³⁴ weeks of gestation. Nangia et al²² reached a similar conclusion in non-vigorous newborns of³⁷ weeks of gestation. Therefore, it is possible that endotracheal suctioning only benefits very selected newborns. Future studies could seek to identify those newborns.

This study had limitations. Although several studies were initially identified, the strict inclusion criteria resulted in only 12 studies being included. Since a preliminary search revealed small numbers of RCTs and cohort studies, both study types were included, resulting in biases based on the analysis of the different data types. In addition, heterogeneity was high, even after excluding the study by Al Takroni et al.¹⁶ A better level of evidence could still be necessary to reach firm conclusions on endotracheal suctioning in neonates born through MSAF.

Conclusion

Routine endotracheal suctioning at birth shows no obvious benefit for preventing MAS, mortality, mechanical ventilation, PPHN, HIE, and prolonged length of stay in neonates born through MSAF.

Data Availability Statement

The data used to support the findings of this study are available from the corresponding author upon request.

Authors' Contributions

Q.W. substantially contributed to the conception or design, acquisition, analysis, and interpretation of data. WC contributed to acquisition, analysis, interpretation of data, and drafted the manuscript for important content. QL critically revised the manuscript for important intellectual content. SS gave final approval. JL contributed to acquisition, analysis, and interpretation of data.

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Conflict of Interest

None declared.

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