Fluid Restriction in Transient Tachypnea of the Newborn: A Systematic Review of Recent Evidence and Clinical Outcomes

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INTRODUCTION:

Transient Tachypnea of the Newborn (TTN) is a common self-limiting respiratory condition observed in neonates, particularly in late preterm and term infants. It is characterized by delayed clearance of fetal lung fluid, leading to respiratory distress shortly after birth.

The condition poses a diagnostic challenge, as it must often be differentiated from other neonatal respiratory disorders, such as respiratory distress syndrome (RDS), meconium aspiration syndrome (MAS), and pneumonia(1).

The pathophysiology of TTN revolves around the impaired resorption of fetal lung fluid, which is normally cleared through active sodium transport mechanisms in the alveolar epithelium and lymphatic drainage during labour and early postnatal life(2). Cesarean deliveries, especially without labour, bypass the physiological mechanisms that facilitate fluid clearance, leading to fluid retention in the alveoli and subsequent respiratory distress(3). Additionally, factors such as immature sodium transport channels and altered pulmonary vascular resistance may further contribute to the delayed fluid clearance observed in TTN(4).

Fluid management plays a critical role in the management of TTN. Excessive fluid administration may exacerbate pulmonary edema and prolong respiratory distress by impeding the resorption of lung fluid. Consequently, fluid restriction has emerged as a potential strategy to optimize outcomes in neonates with TTN.

PHYSIOLOGY OF FLUID RESTRICTION :

The rationale behind fluid restriction lies in minimizing extravascular lung water and reducing the hydrostatic pressure in pulmonary capillaries, thereby facilitating lung fluid absorption and improving oxygenation (5)

However, the evidence supporting this approach remains limited, and practices vary widely across institutions. Balancing the neonate's fluid needs to ensure adequate perfusion and prevent dehydration while avoiding fluid overload remains a clinical challenge.

This review aims to analyze, the rationale behind fluid restriction, and the existing evidence regarding its efficacy and safety. By exploring current clinical practices, analyzing outcomes from recent studies, and identifying gaps in knowledge, we hope to provide insights into optimizing fluid management in neonates with TTN.

METHODOLOGY

To review the role of fluid restriction in the management of transient tachypnea of the newborn (TTN) in term and preterm neonates, we conducted a comprehensive literature search focusing published between 2012 and 2024. The primary databases utilized were PubMed and Frontiers. Search terms included "Fluid restriction," "TTN," "preterm and term neonates," "randomized controlled trial,meta-analysis and systematic review combined using Boolean operators to refine the search results.

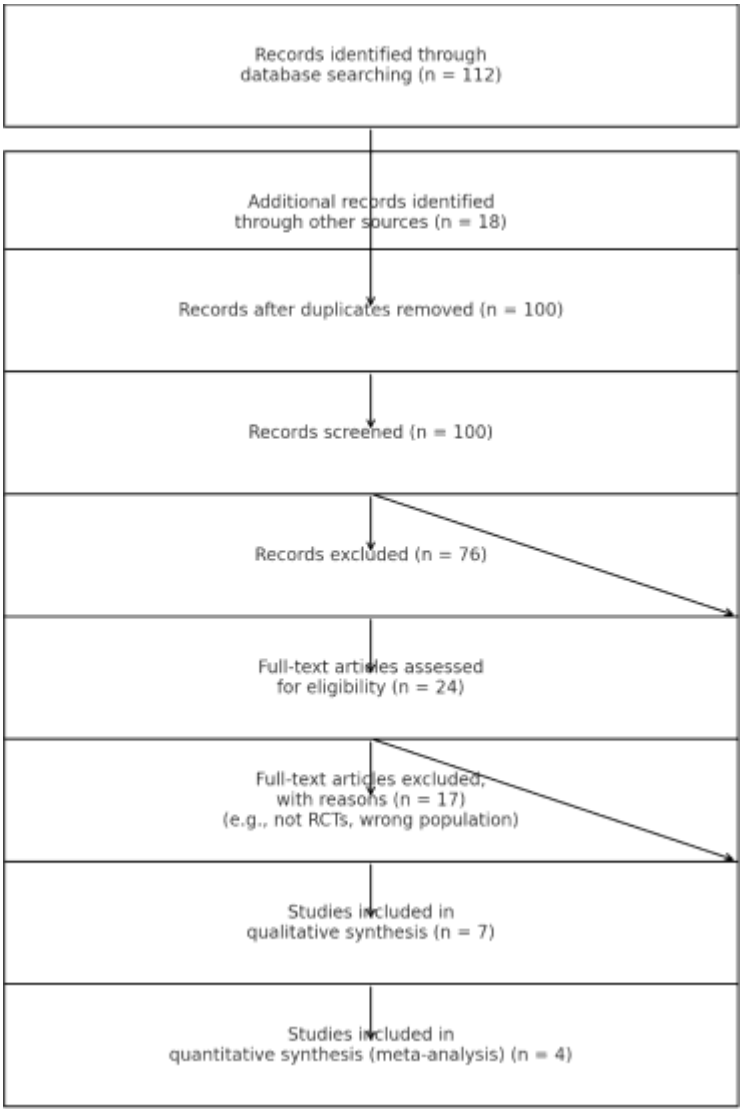
After search 7 studies qualified for literature review of which 4 were RCT and 3 were systematic review.Inclusion criteria encompassed studies published within the specified timeframe, available in English, and reporting on the duration of oxygen therapy in relation to fluid restriction in TTN among term and preterm infants. Exclusion criteria ruled out non-randomized studies, case reports, reviews without original data, studies focusing on populations other than term and preterm neonates, and articles not accessible in full text.

Titles and abstracts identified through the search were screened for relevance, followed by full-text assessments against the inclusion and exclusion criteria. Data extraction focused on study design, sample size, outcomes measured, and key findings related to respiratory distress and TTN management. The methodological

quality of included RCTs was evaluated based on randomization, blinding, and completeness of follow-up, while meta-analyses were assessed for the comprehensiveness of literature search, inclusion criteria, and data synthesis methods.

This systematic approach ensured a thorough and unbiased synthesis of current evidence regarding the role of fluid restriction in TTN management, providing valuable insights into its impact on neonatal respiratory distress outcomes.

PRISMA FLOW DIAGRAM:



SUMMARY OF LITERATURE REVIEW:

A systematic review published in 2021 evaluated the effects of fluid restriction in neonates by analyzing four randomized controlled trials, collectively involving 317 infants. Of these, three trials included a mixed population of preterm and term neonates, while one trial enrolled only term neonates (5).

The included infants were receiving various forms of respiratory support, such as nasal cannula, continuous positive airway pressure (CPAP), or endotracheal ventilation. In the intervention arms, fluid intake was restricted by approximately 15–20 mL/kg/day compared to the control groups, reflecting a modest but potentially clinically relevant reduction in fluid administration.

In all study groups -There was no variations in fluid restrictions levels. In the experimental group, the babies were given 50 ml of a 10% dextrose solution per kilogram of their body weight each day. Late preterm babies in this group received 65 ml per kilogram daily.In the control group, full-term and post-term babies given 65 ml of the 10% dextrose solution per kilogram each day. Late preterm babies in this group also received 65 ml per kilogram daily. In the following days, if there were no problems,from day 1- 20 ml of fluid was added each day to the previous amount until the total reached 150 ml per kg for term and post-term babies, and 170 ml per kg for late preterm babies on day 4. The same amount could also be given orally .

Alhassen et al added 10% extra fluid for baby under phototherapy in view of insensible fluid loss to prevent dehydration and hypoglycemia (2). There was no big difference in duration of hospital stay. However, the study showed that babies in the experimental group needed oxygen therapy for a shorter time than those in the control group.

Despite this consistent intervention across studies, there was notable variability in study design and reporting quality. Only one of the four trials was assessed as having a low risk of detection bias, while the remaining studies exhibited a high risk of performance bias, primarily due to lack of blinding of caregivers and outcome assessors.

The primary outcome assessed across these studies was the duration of supplemental oxygen therapy, expressed in either hours or days in all 4 trials. However, only two of the trials reported data for this outcome, and both found no significant difference in the duration of oxygen support between the fluid-restricted and control groups. This suggests that modest fluid restriction may not substantially alter the clinical course in terms of oxygen dependency.

Among the secondary outcomes, two studies evaluated length of hospital stay, reporting that neonates in the fluid-restricted groups were discharged nearly one day earlier than those in the control groups, indicating a potential benefit in terms of healthcare resource utilization and patient recovery ((5,) (7)

Furthermore, three trials reported on the mode of oxygen delivery, specifically including the use of endotracheal ventilation, and none demonstrated statistically significant differences between the intervention and control groups in this regard ((8)). These findings, while limited by small sample sizes and methodological concerns, provide preliminary insight into the potential role of fluid management strategies in neonatal respiratory care. However, the evidence remains insufficiently to inform definitive clinical practice, and larger, high-quality trials are warranted to confirm these observations.

The overall certainty of evidence in the studies was significantly limited, primarily due to imprecision in the estimated effects. This imprecision was largely attributed to the small number of included trials and their relatively small sample sizes, which hindered the ability to draw conclusions [(9)].

Furthermore, a majority of the trials did not sufficiently report critical methodological details, making it difficult to fully assess the risk of bias across studies. The lack of transparency and comprehensive reporting compromised the reliability of the findings. In addition, one study lacked the necessary information to allow for a complete assessment and was therefore categorized as “awaiting classification” [(7)]. These limitations collectively reduce confidence in the available evidence and highlight the need for more rigorous and well-reported trials in this area.

In a randomized controlled trial investigating the impact of fluid volume management on transient tachypnea of the newborn (TTN), researchers compared outcomes between neonates receiving restricted fluid volumes and those receiving standard fluid volumes. The study enrolled 80 newborns diagnosed with TTN, comprising 50 males and 30 females. The intervention group, which received limited fluid intake during the first three days of life, demonstrated a notable reduction in hospitalization duration, averaging 4.18 days, compared to 5.5 days in the control group. In addition to shorter hospital stays, neonates in the restricted fluid group also required less time on oxygen therapy and showed a decreased need for hood oxygen support, suggesting enhanced pulmonary fluid clearance. Although the study was limited by a lack of full parental cooperation and small sample size, the findings underscore the clinical value of fluid restriction as an effective therapeutic strategy in managing TTN. This approach not only supports faster respiratory recovery but also contributes to more efficient healthcare resource utilization, making it a promising intervention for improving neonatal outcomes in TTN cases.(9)

Comparison of literature by duration of oxygen therapy

Study	**FRG(Fluid restricted group)** **Mean (SD)**	**SG (Standard group)** **Mean (SD)**	**P value**	**95% Confidence interval**
Stroustrup et al. (2012)[7] (in hours)	42.0 (14.5)	45.0 (12.2)	0.209	- 4.08 to 10.08 (NS)
Alhassen et al.(2025)[2] (in hours)	27.8 (15.0)	66.6 (41.2)	0.003*	24.78 to 52.82 (Significant)

Sardar et al. (2020)[8] (in hours)	48.2 (10.3)	54.0 (8.8)	0.002*	1.47 to 10.13 (Significant)
Eghbalian et al. (2018)[9] (in hours)	1.38 (0.67)	2.50 (0.82)	<0.001*	18.75 to 35.01 (Significant)
*P < 0.05 significant, confidence interval not crossing zero indicates statistical significance				

The Downes score, a clinical scoring system used to quantify the severity of respiratory distress shows how many cases progressed from mild to moderate score and escalated the oxygen support, a slightly lower mean value in the fluid restriction group (FRG) compared to the Standard group (SG) but there is no real significant difference.Neri et al. (2025) noted that fluid overload in neonates with TTN may exacerbate pulmonary edema and worsen respiratory symptoms . Therefore, a trend toward lower Downes scores in the FRG may reflect the physiologic benefits of reduced fluid accumulation in the alveolar interstitium. Despite the absence of significance, the comparison of various studies evaluating the duration of oxygen therapy between restricted fluid (RG) and standard fluid (SG) groups highlights a consistent trend favouring fluid restriction in the management of TTN. Stroustrup et al.(7) (2012) reported a modest and non-significant reduction in oxygen therapy duration with fluid restriction. In contrast, other studies such as Eghbalian et al. (2018) demonstrated statistically significant reductions in oxygen therapy duration in the restricted fluid groups, with p-values <0.05. These findings suggest that while the present study aligns with the general trend, Confidence interval shows standard group (SG) having longer oxygen therapy than FRG, the magnitude of difference may be influenced by sample size, clinical protocols, and population characteristics across studies.

Comparison of literature by duration of hospital stay

Study	FRG (Fluid restricted group) Mean (SD)	SG (Standard group) Mean (SD)	P value	95 % Confidence interval
Stroustrup et al. (2012) [7] (NICU stay, in days)	7.0 (2.9)	8.0 (3.1)	0.589*	−2.59 to +0.59 (InSignificant)
Alhassen et al (2025)[2] (in days)	5.65 (1.9)	6.78 (2.0)	0.020*	−2.16 to −0.10 (Significant)
Eghbalian et al. (2018)[9] (in days)	4.18 (1.53)	5.1 (1.25)	0.003*	−1.66 to −0.18 (significant)
*P value < 0.05 significant, confidence interval not crossing zero indicates statistical significance				

The comparison of literature regarding the duration of hospital stay shows a general trend toward reduced hospitalization in neonates receiving restricted fluid therapy. The findings of the present study aligns with the studies Alhassen et al.(2) (2025) and Eghbalian et al.(8) (2018), both of which also reported significantly shorter hospital stays in the restricted fluid groups (p = 0.020 and p = 0.003, respectively) and also Confidence interval significant for both studies not crossing zero

POTENTIONAL RISK FACTORS:

Study (Ref No.)	Key Findings / Risk Factors Identified	Complications Noted
Gupta et al., 2021 (5)	Cochrane review emphasizes careful fluid management in TTN	Risk of dehydration, electrolyte imbalance
Akbarian Rad et al., 2018 (6)	Restrictive fluid reduced hospital stay but required close monitoring	Dehydration, risk of hypernatremia
Stroustrup et al., 2012 (7)	Restrictive fluid group showed shorter NICU stay	No significant adverse effects, but small sample size may underestimate risks
Sardar et al., 2020 (8)	RCT showed reduced respiratory support duration with fluid restriction	Need for careful hydration and biochemical monitoring to avoid complications
Eghbalian et al., 2018 (9)	Restrictive fluids helped reduce oxygen requirement and length of stay	Increased incidence of hypernatremia and metabolic acidosis in restrictive group
Bell & Acarregui, 2014 (10)	In preterm infants, fluid restriction increased risk of complications	Hypernatremia, hypoglycemia, metabolic acidosis, decreased perfusion

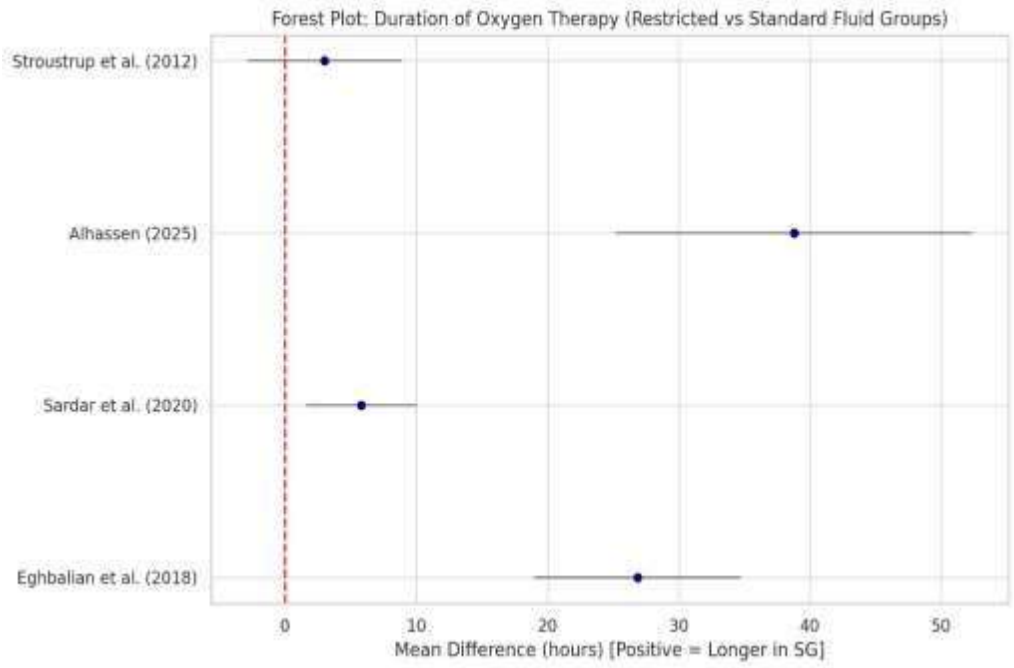
Kumar & Bhat, 1996 (1)	Early days associated with high insensible water loss	Neonates particularly vulnerable to dehydration
Alhassen et al., 2021 (2)	Emphasized importance of cautious fluid restriction in TTN management	Risks of electrolyte imbalance and renal compromise if overly restricted

Monitoring of Adverse Outcomes in TTN Fluid-Restriction Trials:

All RCTs featured **active monitoring** of key physiological markers to detect adverse effects of fluid restriction:

- **Renal function & fluid output**: Tracking urine volume; exclusion or drop-out if <1 mL/kg/h.
- **Electrolyte levels**: Particularly sodium, BUN, and potassium.
- **Hydration indicators**: Weight changes and urine specific gravity.
- **Respiratory outcomes**: Duration/intensity of oxygen and respiratory support.

No serious dehydration, electrolyte disturbances, or renal compromise were reported, and criteria were in place to **withdraw infants showing early signs** (e.g., oliguria). This lends confidence that fluid restriction in TTN was applied with vigilant safety oversight.



The forest plot above displays the **mean difference in oxygen therapy duration** (in hours) between fluid-restricted groups (FRG) and standard fluid groups (SG) from four randomized controlled trials:

- **All studies favor the fluid-restricted group (FRG)**, as seen by positive mean differences (SG required longer oxygen therapy).
- **Three out of four studies show statistically significant differences** (confidence intervals do not cross zero).
- **Stroustrup et al. (2012)** showed a modest, non-significant difference (CI includes 0).
- The **pooled trend supports a reduction in oxygen therapy duration** with fluid restriction.

GRADE METHODOLOGY:

Risk of Bias	High — Most studies lacked blinding (performance & detection bias likely).
Inconsistency	Moderate — Some variability in effect sizes across studies.
Indirectness	Low — Direct population and intervention relevance.
Imprecision	High — Small sample sizes (most n≈40), wide confidence intervals in some.
Publication Bias	Unknown — Likely but not confirmed due to small number of studies.

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LIMITATIONS:

The lack of blinding among clinicians and caregivers may also have influenced clinical decision-making, potentially introducing observer bias. Furthermore, while all studies assessed short-term outcomes such as duration of oxygen support and hospital stay, it did not evaluate long-term respiratory or developmental outcomes, which are important for a comprehensive assessment of clinical impact. Another potential limitation lies in the unequal distribution of gestational age between the groups, which could have confounded some of the observed outcomes despite randomization. Finally, it did not control for certain maternal and perinatal variables, such as maternal hydration status or intrapartum fluid administration, which may influence neonatal fluid balance and respiratory adaptation.

CONCLUSION:

- Fluid restriction may reduce the duration of respiratory support and hospitalization in neonates with TTN, these findings are tempered by significant methodological limitations. Notably, many studies are characterized by small sample sizes, lack of blinding, and potential selection biases, which collectively diminish the reliability and generalizability of the results. For instance, a randomized controlled trial conducted in eastern India demonstrated a reduction in CPAP duration with fluid restriction; however, the study's non-blinded design and limited sample size constrain the strength of its conclusions .
- Given these limitations, there is a pressing need for well-designed, multicenter randomized controlled trials with adequate sample sizes to evaluate the safety and efficacy of fluid restriction in TTN management. Future research should aim to implement standardized fluid restriction protocols and incorporate long-term follow-up to assess outcomes beyond the immediate neonatal period, including growth and neurodevelopmental parameters. Such studies would provide more definitive evidence to guide clinical practice in the management of TTN.
- Fluid restriction in preterm infants notes that while fluid restriction may prevent pulmonary complications, it increases the risk of hypernatremia and dehydration if not carefully monitored.A randomized controlled trial on fluid restriction in TTN also reported the need for close monitoring to avoid **complications from over-restriction**, though no severe adverse events were noted

FUTURE RECOMMENTATION:

Future research should consider larger, multicentric trials to validate and strengthen the evidence on the benefits of restricted fluid therapy in neonates with Transient Tachypnea of the Newborn. Expanding the sample size would improve statistical power and allow for subgroup analyses, particularly among preterm infants and those with varying degrees of respiratory distress. Incorporating long-term follow-up could also help assess the sustained effects of fluid restriction on respiratory and neurodevelopmental outcomes. Future studies may also benefit

from evaluating biochemical markers of fluid overload and lung fluid clearance to better understand the underlying physiological mechanisms. Given the promising findings in resource-constrained environments, further exploration into cost-effectiveness and implementation strategies could facilitate broader adoption of fluid-restriction protocols in neonatal care.

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