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COMPARISON OF EFFICACY OF PHOTOTHERAPY PLUS ALBUMIN VS PHOTOTHERAPY ALONE IN BABIES WITH NEONATAL JAUNDICE

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ABSTRACT

Background: Neonatal jaundice is one of the most common clinical conditions requiring medical attention during the neonatal period. Although phototherapy is the standard treatment for unconjugated hyperbilirubinemia, adjunctive therapies such as albumin infusion may enhance bilirubin reduction by increasing bilirubin-binding capacity and facilitating its clearance.

Objective: To compare the efficacy of phototherapy plus albumin infusion versus phototherapy alone in neonates with neonatal jaundice.

Methods: This randomized controlled trial was conducted in the Department of Pediatrics, Allied Hospital Faisalabad, from 12 February 2026 to 12 May 2026. A total of 620 neonates with neonatal jaundice requiring treatment were enrolled and randomly allocated into two equal groups. Group A (n=310) received standard phototherapy alone, whereas Group B (n=310) received phototherapy plus intravenous human albumin infusion at a dose of 1.5 g/kg during the first two hours of treatment. Serum total bilirubin levels were measured before treatment and after completion of therapy. Treatment efficacy was assessed based on a clinically significant reduction in serum bilirubin levels. Data were analyzed using SPSS version 25.0, and treatment efficacy was compared between groups using the Chi-square test.

Results: Baseline demographic and clinical characteristics, including age, gender, weight, family history of jaundice, and pre-treatment serum bilirubin levels, were comparable between the two groups **(**$p > 0.05$**).** The mean post-treatment serum bilirubin level was significantly lower in the phototherapy-plus-albumin group than in the phototherapy-alone group (10.8 ± 1.7 vs. 14.3 ± 1.9 mg/dL; $p < 0.001$**).** The mean reduction in serum bilirubin was also significantly greater with combination therapy (7.9 ± 1.5 vs. 4.1 ± 1.3 mg/dL; $p < 0.001$). Treatment efficacy was significantly higher in Group B **(**44.5%, 138/310**)** than in Group A **(**21.6%, 67/310**;** $\chi^2 = 36.74$, $p < 0.001$**).**

Conclusion: Phototherapy combined with albumin infusion was significantly more effective than phototherapy alone in reducing serum bilirubin levels among neonates with jaundice. Albumin may provide additional bilirubin-lowering benefit when used as an adjunct to phototherapy in appropriately selected neonates with significant hyperbilirubinemia. However, further studies evaluating unbound bilirubin, safety outcomes, and long-term neurological effects are warranted.

KEYWORDS: Neonatal Jaundice, Hyperbilirubinemia, Phototherapy, Albumin Infusion, Serum Bilirubin.

INTRODUCTION

An increased bilirubin level in a newborn's blood is known as neonatal jaundice (NJ) (Ahmed et al., 2020; Hansen, 2021). It typically manifests in the first few days of life and affects 80% of newborns (Tessema et al., 2024; Zinjani, 2023). Jaundice is the most common aberrant clinical feature among newborn illnesses that requires hospital admission or readmission during the first week of life (Jha et al., 2022; Ansong-Assoku et al., 2024; Blumovich et al., 2020). Unconjugated hyperbilirubinemia is normal in the majority of babies, but excessive bilirubin concentration can cause bilirubin encephalopathy and, in extreme situations, kernicterus, which can result in lasting neurological deficits (Jayanti et al., 2021; Qian et al., 2022; Shapiro & Riordan, 2020). Therefore, in order to avoid major consequences, early detection and appropriate treatment of newborn hyperbilirubinemia are crucial (Hansen et al., 2020).

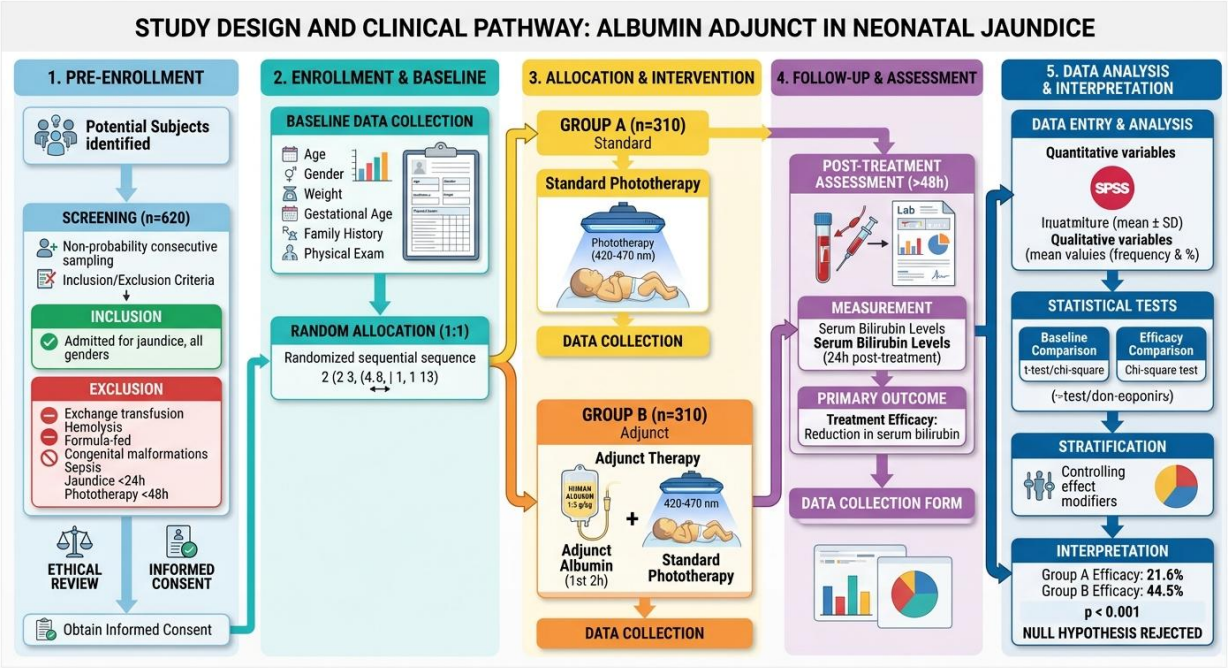
About 10% of affected neonates need active therapy because of significantly high bilirubin levels, despite the fact that NJW can result from a range of etiological reasons and frequently resolves on its own without intervention (Zhang et al., 2022; Wickremasinghe & Kuzniewicz, 2025). Severe hyperbilirubinemia can cause neuronal damage if treatment is not received, which can result in issues like cerebral palsy, hearing loss, or vision impairment (Gazzin et al., 2023).

The primary treatment for unconjugated hyperbilirubinemia is still phototherapy, which changes bilirubin into photoisomers that are eliminated in urine (Fouly et al., 2024; Lindqvist et al., 2025). As an adjuvant, albumin infusion increases the effectiveness of phototherapy by binding bilirubin and lowering unbound levels (Bibi et al., 2020). Research indicates that 10% albumin may have neuroprotective advantages in cases of severe

hyperbilirubinemia, whereas 25% albumin speeds up the bilirubin drop during the first 24 hours (Elshenawi et al., 2021).
Caldera et al. (1993) assessed the efficacy of phototherapy combined with albumin infusion. Infants in the albumin group received additional human albumin (1.5 g/kg) during the first 2 hours. After 4 hours, serum efficacy (in terms of bilirubin reduction) was 45%, while another study reported 22% efficacy of phototherapy alone (Fatima et al., 2021).
Neonatal jaundice is among the most frequent causes of hospital admission (Diala et al., 2023). Although phototherapy remains the mainstay of treatment for unconjugated hyperbilirubinemia, its effect may be limited in cases with rapidly rising or very high bilirubin levels (Wang et al., 2021). International studies have shown that adding albumin infusion to phototherapy can accelerate the early decline of bilirubin; however, local evidence is limited and outdated, and clinical benefit in our population has not been adequately established (Caldera et al., 1993; Kamyab et al., 2025). This study aims to evaluate the efficacy of phototherapy with albumin infusion compared to phototherapy alone in reducing serum bilirubin levels in neonates with jaundice. The results will contribute to the development of evidence-based guidelines to improve neonatal outcomes and reduce morbidity and mortality associated with severe jaundice.

Objective
To compare efficacy of Phototherapy Plus Albumin versus Phototherapy alone in babies with Neonatal Jaundice

METHODOLOGY
This randomized controlled trial was conducted in the Department of Pediatrics, Allied Hospital Faisalabad, from 12 February 2026 to 12 May 2026 to compare the efficacy of phototherapy plus albumin infusion versus phototherapy alone in neonates with neonatal jaundice. A total of 620 neonates diagnosed with jaundice and requiring treatment were enrolled using a non-probability consecutive sampling technique**.** The sample comprised 310 participants in each group**.** Neonates of either gender who were admitted for the treatment of jaundice were included in the study. Infants who had undergone exchange transfusion, had evidence of hemolysis, were formula-fed, had congenital malformations, proven sepsis or infection, jaundice appearing within the first 24 hours of life, or received phototherapy for less than 48 hours were excluded.
The study commenced after obtaining approval from the Ethical Review Committee (ERC) and the College of Physicians and Surgeons Pakistan (CPSP). Written informed consent was obtained from the parents or legal guardians of all eligible neonates before enrollment. Baseline demographic and clinical information, including age, gender, weight, gestational age, and family history of jaundice, was recorded through a structured proforma. A detailed physical examination was performed for each participant. Eligible neonates were then randomly allocated into two equal groups using a computer-generated randomization sequence. Group A (n=310) received standard phototherapy alone, whereas Group B (n=310) received phototherapy along with intravenous human albumin infusion at a dose of 1.5 g/kg administered during the first two hours of treatment.
Phototherapy was provided using blue fluorescent light with a wavelength range of 420–470 nm, positioned approximately 15–20 cm above the neonate according to standard neonatal care protocols. Serum total bilirubin levels were measured before initiation of therapy and again 24 hours after completion of treatment. The primary outcome measure was treatment efficacy, determined by the reduction in serum bilirubin levels following the intervention. All observations and laboratory findings were documented on a specially designed data collection form.
Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 25.0. Quantitative variables such as age, weight, and serum bilirubin levels were presented as mean ± standard deviation, while qualitative variables including gender, family history of jaundice, and treatment efficacy were expressed as frequencies and percentages. The Chi-square test was used to compare treatment efficacy between the two study groups. Potential effect modifiers such as age, gender, weight, gestational age, and family history of jaundice were controlled through stratification, followed by post-stratification Chi-square analysis. A p-value of ≤ 0.05 was considered statistically significant.



RESULTS

A total of 620 neonates with neonatal jaundice were enrolled in the study and randomly allocated into two equal groups, with 310 participants in each group. Group A received phototherapy alone, while Group B received phototherapy plus albumin infusion. The baseline demographic and clinical characteristics of the participants, including age, gender, weight, family history of jaundice, and pre-treatment serum bilirubin levels, were comparable between the two groups ($p > 0.05$).

Table 1. Baseline Characteristics of Study Participants

Variable	Group A (Phototherapy Alone) n=310	Group B (Phototherapy + Albumin) n=310	p-value
Age (days), Mean ± SD	5.2 ± 1.8	5.4 ± 1.9	0.14
Weight (kg), Mean ± SD	3.1 ± 0.4	3.2 ± 0.5	0.08
Male Gender, n (%)	176 (56.8)	186 (60.0)	0.42
Family History of Jaundice, n (%)	71 (22.9)	81 (26.1)	0.38
Baseline Bilirubin (mg/dL), Mean ± SD	18.4 ± 2.1	18.7 ± 2.3	0.09

The mean serum bilirubin level before treatment was comparable between the two groups. Following treatment, a greater reduction in serum bilirubin was observed among neonates receiving phototherapy plus albumin compared with those receiving phototherapy alone.

Table 2. Comparison of Serum Bilirubin Levels

Variable	Group A (Phototherapy Alone) n=310	Group B (Phototherapy + Albumin) n=310	p-value
Baseline Bilirubin (mg/dL)	18.4 ± 2.1	18.7 ± 2.3	0.09
Post-treatment Bilirubin (mg/dL)	14.3 ± 1.9	10.8 ± 1.7	<0.001
Mean Reduction (mg/dL)	4.1 ± 1.3	7.9 ± 1.5	<0.001

Treatment efficacy was assessed based on a clinically significant reduction in serum bilirubin levels after therapy. The efficacy rate in Group A was 21.6% (67/310), whereas the efficacy rate in Group B was 44.5% (138/310). The difference between the two groups was statistically significant ($\chi^2 = 36.74$, $p < 0.001$).

Table 3. Comparison of Efficacy between Study Groups

Efficacy	Group A (Phototherapy Alone) n=310	Group B (Phototherapy + Albumin) n=310	Total
Effective	67 (21.6%)	138 (44.5%)	205
Not Effective	243 (78.4%)	172 (55.5%)	415
Total	**310 (100%)**	**310 (100%)**	**620**

Chi-square test: $\chi^2 = 36.74$
p-value: <0.001

The findings demonstrated that phototherapy combined with albumin infusion was significantly more effective than phototherapy alone in reducing serum bilirubin levels among neonates with jaundice. Neonates treated with adjunctive albumin therapy showed a greater decline in bilirubin concentration and a higher overall treatment success rate. Therefore, the null hypothesis was rejected, and the alternate hypothesis was accepted, indicating a statistically significant difference in efficacy between the two treatment modalities.

DISCUSSION

Neonatal jaundice remains one of the most common clinical conditions requiring medical attention during the early neonatal period. Although physiological jaundice resolves spontaneously in most newborns, severe unconjugated hyperbilirubinemia can lead to acute bilirubin encephalopathy and kernicterus if not appropriately managed. Phototherapy remains the standard treatment for neonatal hyperbilirubinemia because it converts unconjugated bilirubin into water-soluble photoisomers that can be eliminated without hepatic conjugation (Anderson & Calkins, 2020). However, in neonates with significant hyperbilirubinemia, adjunctive interventions such as albumin infusion have been investigated to improve bilirubin binding and facilitate its clearance (Hansen et al., 2020; Gazzin et al., 2023).

The present randomized controlled trial evaluated the efficacy of phototherapy combined with albumin infusion compared with phototherapy alone among 620 neonates with neonatal jaundice, with 310 participants allocated to each treatment group. The baseline demographic and clinical characteristics were comparable between the groups, indicating adequate baseline comparability. The findings demonstrated a significantly greater reduction in serum bilirubin among neonates who received phototherapy plus albumin compared with those who received phototherapy alone. The mean bilirubin reduction was 7.9 ± 1.5 mg/dL in the combination-therapy group compared with 4.1 ± 1.3 mg/dL in the phototherapy-alone group ($p < 0.001$). Similarly, the treatment efficacy rate was substantially higher in the combination group (44.5%, 138/310) than in the phototherapy-alone group (21.6%, 67/310), with the difference being statistically significant ($\chi^2 = 36.74$, $p < 0.001$).

The greater reduction in serum bilirubin observed with combination therapy may be explained by the physiological role of albumin in bilirubin transport. Unconjugated bilirubin circulates predominantly bound to albumin, and the unbound fraction is considered particularly relevant to bilirubin neurotoxicity. Administration of albumin may increase the available bilirubin-binding capacity in plasma, thereby facilitating the movement of bilirubin from tissues into the intravascular compartment, where it can subsequently undergo photochemical conversion and elimination. This mechanism may account for the more pronounced reduction in bilirubin observed in the present study.

The efficacy rate of 44.5% observed in the phototherapy-plus-albumin group was comparable to the approximately 45% efficacy reported by Caldera et al. (1993), who evaluated human albumin administration in conjunction with intensive phototherapy in neonates with severe hyperbilirubinemia. Their findings similarly suggested a more rapid decline in bilirubin concentrations with adjunctive albumin therapy. The consistency between these findings and the present results provides support for the potential role of albumin in enhancing bilirubin reduction when used alongside phototherapy. Nevertheless, differences in study populations, definitions of treatment success, bilirubin thresholds, albumin dosing, and phototherapy protocols should be considered when comparing efficacy estimates across studies.

In the present study, phototherapy alone resulted in a treatment efficacy rate of 21.6%, indicating that conventional phototherapy remained beneficial but was less effective than the combined intervention under the conditions of this trial. Fatima et al. (2021) similarly reported that conventional phototherapy was effective in reducing bilirubin levels among neonates with unconjugated hyperbilirubinemia, although the response may vary according to the severity of jaundice and other clinical factors. The current findings therefore reinforce the established role of phototherapy as the primary treatment modality while suggesting that adjunctive albumin may provide additional benefit in appropriately selected neonates.

The magnitude of bilirubin reduction further supports the observed difference in treatment efficacy. Neonates receiving phototherapy plus albumin demonstrated a mean reduction of 7.9 mg/dL, compared with 4.1 mg/dL among those receiving phototherapy alone. In addition to the statistically significant difference, the larger absolute reduction observed with combination therapy suggests a potentially clinically relevant improvement in bilirubin clearance. However, statistical significance alone does not establish that albumin therapy prevents neurological complications, particularly because the present study did not directly assess unbound bilirubin concentrations or long-term neurological outcomes.

Hansen et al. (2020) emphasized the importance of the unbound fraction of bilirubin in bilirubin-induced neurological injury. From a physiological perspective, increasing albumin availability could potentially reduce the concentration of circulating unbound bilirubin by increasing bilirubin-binding capacity. However, the present study measured total serum bilirubin rather than unbound bilirubin. Therefore, although the observed reduction in total bilirubin is consistent with a potential improvement in bilirubin binding and elimination, a direct neuroprotective effect of albumin cannot be established from the present findings.

The results also have potential clinical implications. The statistically significant difference in treatment efficacy between the two groups, observed in a relatively large sample of 620 neonates, suggests that albumin may have value as an adjunct to phototherapy in selected cases of significant neonatal hyperbilirubinemia. Nevertheless, albumin should not be interpreted as a replacement for established phototherapy protocols. Its use should be

considered in the context of clinical severity, bilirubin levels, gestational age, albumin status, and institutional treatment protocols. Careful patient selection is particularly important because albumin infusion involves additional cost, intravenous administration, and potential treatment-related risks.

Several limitations should be considered when interpreting these findings. First, the study was conducted at a single tertiary-care hospital, which may limit the generalizability of the results to other hospitals and neonatal populations. Second, the follow-up period was limited to the immediate treatment period, and long-term neurological outcomes were not evaluated. Third, unbound bilirubin concentrations were not measured; therefore, the study could not directly determine whether albumin infusion reduced the neurotoxic fraction of bilirubin. Fourth, other potentially relevant factors influencing treatment response, such as detailed nutritional status, serum albumin concentration, bilirubin production rate, and variations in phototherapy intensity, were not comprehensively evaluated. Finally, although the larger sample size provided greater precision in estimating the treatment difference, the findings remain specific to the treatment protocol and patient population studied.

Future multicenter randomized controlled trials should evaluate the effectiveness and safety of albumin-assisted phototherapy in different neonatal populations and clinical settings. Such studies should incorporate measurements of serum albumin and unbound bilirubin, standardized phototherapy protocols, assessment of adverse events, and longer-term neurological follow-up. These investigations would help determine which neonates are most likely to benefit from adjunctive albumin therapy and whether the observed reduction in bilirubin translates into meaningful clinical benefits.

Overall, the present study demonstrated that phototherapy combined with albumin infusion produced a significantly greater reduction in serum bilirubin and a higher treatment efficacy rate than phototherapy alone. The findings support the potential role of albumin as an adjunctive intervention in carefully selected neonates with significant hyperbilirubinemia, while further evidence is required before its routine use can be recommended across all cases of neonatal jaundice.

CONCLUSION

The present randomized controlled trial involving 620 neonates demonstrated that phototherapy combined with albumin infusion was significantly more effective than phototherapy alone in reducing serum bilirubin levels among neonates with neonatal jaundice. The combination-therapy group showed a greater mean reduction in bilirubin (7.9 ± 1.5 mg/dL vs. 4.1 ± 1.3 mg/dL) and a higher treatment efficacy rate (44.5% vs. 21.6%), with the difference being statistically significant ($p < 0.001$).

These findings suggest that albumin infusion may enhance the bilirubin-lowering effect of phototherapy, potentially through increased bilirubin-binding capacity and facilitation of bilirubin redistribution and elimination. However, the study did not directly assess unbound bilirubin or long-term neurological outcomes; therefore, a neuroprotective effect cannot be concluded. Albumin may be considered a potentially beneficial adjunct to phototherapy in appropriately selected neonates with significant hyperbilirubinemia, while phototherapy remains the cornerstone of treatment. Further multicenter randomized controlled trials with standardized protocols, assessment of unbound bilirubin, safety outcomes, and long-term follow-up are warranted to establish the clinical role and optimal use of albumin therapy in neonatal jaundice.

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