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Research Article

# Comparison of Total Bilirubin in Small for Gestational Age (SGA) and Appropriate for Gestational Age (AGA) Infants between 48 Hours - 72 Hours

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## Abstract

**Introduction:** Neonatal jaundice is a common clinical condition, particularly prevalent among infants with intrauterine growth restriction. Small for gestational age (SGA) infants are at increased risk for hyperbilirubinemia compared to their appropriate for gestational age (AGA) counterparts. Elevated total serum bilirubin levels in SGA infants may be attributed to factors such as delayed hepatic maturation and increased hemolysis. This study aims to compare total bilirubin levels between SGA and AGA infants at 48 hours post-birth, with additional analysis across subgroups on birth weight, feeding methods, maternal diabetes status, and phototherapy treatment intervention.

**Objectives:** To compare the mean total serum bilirubin levels between SGA and AGA infants at 48 hours post-birth. To analyze differences in bilirubin levels within the SGA and AGA subgroups based on the following subgroups: birth weight (low vs. normal), feeding method (breastfed vs. formula-fed), maternal diabetes status (infants of diabetic mothers (IDMs) vs. non-diabetic mothers), and phototherapy treatment (infants who received phototherapy vs. those who did not).

**Materials and Methods:** This observational study included a total 128 neonates, comprising 64 SGA and 64 AGA infants. Total serum bilirubin levels were measured 48 hours after birth using a direct measurement method. Subgroup analyses were conducted within both the SGA and AGA groups based on the following variables: birth weight (low vs. normal), feeding method (breastfed vs. formula-fed), maternal diabetes status (infants of diabetic mothers vs. non-diabetic mothers), and phototherapy treatment (with vs. without phototherapy). Statistical analyses were performed using independent t-tests and one-way analysis of variance (ANOVA), with a significance threshold set at $p < 0.05$.

**Results:** The mean total bilirubin level was significantly higher in SGA infants (12.5 mg/dL) than in AGA infants (8.7 mg/dL) ($p < 0.001$). Within the SGA group, LBW infants had higher bilirubin levels (13.8 mg/dL) compared to NBW infants (11.2 mg/dL) ($p < 0.01$). SGA formula-fed infants exhibited higher bilirubin levels (13.2 mg/dL) than breastfed SGA infants (11.8 mg/dL) ($p < 0.05$). Additionally, SGA infants born to diabetic mothers had higher bilirubin levels (13.5 mg/dL) than non-diabetic mothers (11.5 mg/dL) ($p < 0.01$). Phototherapy significantly reduced bilirubin levels in both SGA and AGA infants, with SGA infants receiving phototherapy showing a mean bilirubin level of 10.5 mg/dL versus 13.5 mg/dL in those who did not receive phototherapy ($p < 0.001$).

**Conclusion:** SGA infants exhibit significantly higher total bilirubin levels compared to AGA infants, with pronounced differences observed in specific subgroups. LBW SGA infants, formula-fed SGA infants, and SGA infants, and those born to diabetic mothers are particularly at risk for elevated bilirubin levels. Phototherapy is an effective intervention for reducing bilirubin levels in these infants. These findings underscore the importance of targeted bilirubin monitoring and management strategies for SGA infants to prevent complications associated with neonatal jaundice.

**Keywords:** Neonatal Jaundice; Small for Gestational Age (SGA); Appropriate for Gestational Age (AGA); Total Bilirubin Levels; Intrauterine Growth Restriction; Phototherapy; Birthweight; Feeding Methods; Maternal Diabetes; Hyperbilirubinemia

## Introduction

### Background

Neonatal jaundice, characterised by elevated levels of total bilirubin in the blood, is a prevalent condition in newborns. Bilirubin is a pigment produced from the breakdown of red blood cells and is typically processed by the liver for excretion. Elevated bilirubin levels can lead to jaundice, which, if not managed appropriately, may result in serious complications such as kernicterus, a condition where excess bilirubin deposits in the brain, leading to potential long-term neurological damage.

### Small-for-Gestational-Age (SGA) vs. Appropriate-for-Gestational-Age (AGA) infants

Infants categorised as small for gestational age (SGA) have a birth weight below the 10$^{th}$ percentile for their gestational age, indicating growth restriction. In contrast, appropriate-for-gestational-age (AGA) infants have birth weights between the 10$^{th}$ and 90$^{th}$ percentiles. SGA infants are at a higher risk for various complications, including increased bilirubin levels, which can be attributed to factors such as impaired hepatic function and increased red blood cell turnover [1].

### Importance of total bilirubin measurement

Accurate measurement of total bilirubin is critical in diagnosing and managing neonatal jaundice. Elevated bilirubin levels can signify more severe forms of jaundice that may necessitate intervention. Effective management strategies are crucial, particularly for SGA infants who might be predisposed to higher bilirubin levels due to their growth status and potential hepatic immaturity [2].

### Alternative subgroup comparisons

To provide a nuanced understanding of bilirubin levels, this study includes the following alternative subgroups:

- **Birth Weight Classification**: Low Birth Weight (LBW) vs. Normal Birth Weight (NBW): Evaluating the impact of birth weight on bilirubin levels. LBW infants are often more susceptible to higher bilirubin levels due to underdeveloped physiological functions [3].
- **Feeding Method:** Breastfeeding vs Formula Feeding: Investigating the effect of different feeding methods on bilirubin levels. Breastfeeding has been associated with lower bilirubin levels, potentially due to its effects on hydration and digestion frequency [5].
- **Maternal Diabetes Status:** Infants of Diabetic Mothers (IDMs) vs. Non-Diabetic Mothers (non-IDMs): Comparing bilirubin levels between infants born to diabetic mothers and those born to non-diabetic mothers. Maternal diabetes can impact bilirubin metabolism and increase the risk of jaundice [7,8].
- **Exposure to Phototherapy:** Infants Treated vs. Not Treated with Phototherapy: Comparing bilirubin levels in infants who received phototherapy to those who did not. Phototherapy is a common treatment for reducing elevated bilirubin levels [6].

## Aims and Objectives

### Primary objective

To Compare Total Bilirubin Levels Between SGA and AGA Infants at 48 Hours of Life: This primary objective seeks to determine whether there is a significant difference in total bilirubin levels between SGA and AGA infants at 48 hours of life. By comparing these two groups, the study aims to elucidate the impact of growth status on bilirubin levels and assess the relative risk of hyperbilirubinemia associated with being SGA compared to AGA [1].

### Secondary objectives

To Evaluate the Impact of Birth Weight on Total Bilirubin Levels Within the SGA and AGA Groups:

- **Objective:** Assess how birth weight, categorised as low birth weight (LBW) and normal birth weight (NBW), affects bilirubin levels within both SGA and AGA groups [3].
- **Rationale:** LBW infants, irrespective of their growth status, may have higher bilirubin levels due to increased physiological stress and immature liver function. Understanding these differences can help tailor management strategies based on birth weight.

To Investigate the Effect of Feeding Method on Total Bilirubin Levels in SGA and AGA Infants:

- **Objective:** Compare bilirubin levels between breastfed and formula-fed infants within both the SGA and AGA groups [5,6].
- **Rationale:** Breastfeeding has been associated with lower bilirubin levels due to its impact on hydration and bowel movements, which facilitate bilirubin excretion. This objective aims to evaluate whether the feeding method contributes to differences in bilirubin levels between SGA and AGA infants.

To Examine the Influence of Maternal Diabetes Status on Total Bilirubin Levels in SGA and AGA Infants:

- **Objective**: Compare bilirubin levels between infants of diabetic mothers (IDMs) and non-diabetic mothers (non-IDMs) within both SGA and AGA groups [7].
- **Rationale:** Maternal diabetes can affect bilirubin metabolism in newborns, potentially leading to higher bilirubin levels. This objective aims to explore how maternal diabetes status impacts bilirubin levels across different growth statuses.

## Methods

### Study design

This comparative, hospital based observational analysis conducted to evaluate total bilirubin levels in SGA (Small-for-Gestational-Age) and AGA (Appropriate-for-Gestational-Age) infants after 48 hours of life. The study also explored various subgroups to identify factors influencing bilirubin levels.

### Study setting

The study was carried out in the neonatal unit at Srinivas Medical College, ensuring comprehensive data collection and standardized clinical assessment.

### Study population

Sample Size: The study included 128 infants, divided into:

- 64 AGA Infants
- 64 SGA Infants

### Inclusion criteria

- **AGA Infants:** Birth weights between the 10$^{th}$ and 90$^{th}$ percentiles for their gestational age.
- **SGA Infants**: Birth weights below the 10$^{th}$ percentile for their gestational age.
- **Age:** Infants were assessed at 48 hours of life.

### Exclusion criteria

- **Major Congenital Anomalies:** Infants with significant congenital anomalies were excluded to avoid confounding effects on bilirubin levels.
- **Severe Haemolytic Disease:** Infants with severe haemolytic disease were excluded due to its impact on bilirubin levels.

### Data collection

- **Bilirubin Measurement:** Total bilirubin levels were measured at 48 hours of life in a certified laboratory.
- **Gestational Age:** Recorded from delivery records.
- **Birth Weight:** Documented at birth.
- **Feeding Method:** Classified as breastfeeding (exclusive breast milk) or formula feeding (either exclusively or in combination with breastfeeding).
- **Maternal Diabetes Status:** Identified from maternal medical records, classified as:
- **Infants of Diabetic Mothers (IDMs):** Infants born to mothers with diabetes (type 1, type 2, or gestational diabetes).
- **Infants of Non-Diabetic Mothers (non-IDMs):** Infants born to mothers without diabetes.
- **Phototherapy Treatment:** Recorded as received or not received.

### Subgroup classification

Birth Weight Subgroups:

- **Low Birth Weight (LBW):** Infants with birth weight <2500 grams.
- **Normal Birth Weight (NBW):** Infants with birth weight ≥2500 grams.

Feeding Method Subgroups:

- **Breastfeeding:** Exclusive or primary breastfeeding.
- **Formula Feeding:** Exclusive formula feeding or combination feeding.

Maternal Diabetes Status Subgroups:

- **IDMs:** Infants born to mothers with any form of diabetes.
- **Non-IDMs:** Infants born to mothers without diabetes.

Phototherapy Treatment Subgroups:

- **Treated with Phototherapy:** Infants who received phototherapy.
- **Not Treated with Phototherapy:** Infants who did not receive phototherapy.

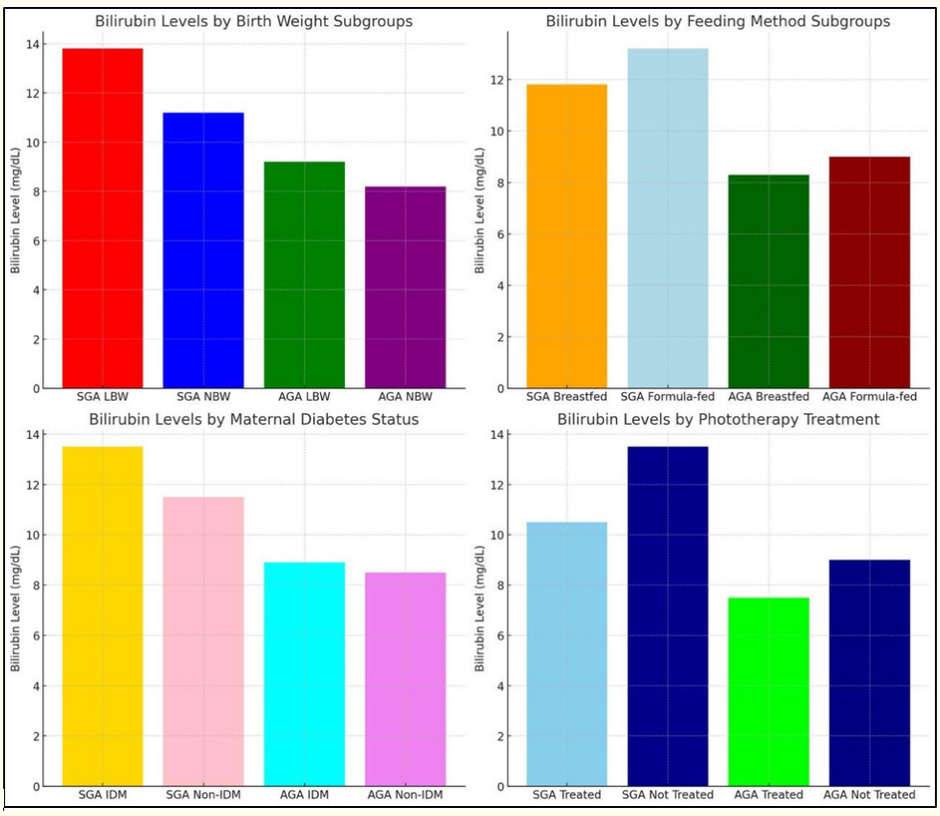


**Figure 1**

### Statistical analysis

- **Descriptive Statistics:** Means, standard deviations, and ranges for total bilirubin levels were calculated for each group and subgroup.

### Comparative analysis

- **Independent Samples t-Test:** Used to compare mean bilirubin levels between SGA and AGA groups, as well as between subgroups within the SGA and AGA groups (e.g., LBW vs. NBW, breastfeeding vs. formula feeding).
- **Mann-Whitney U Test:** Applied for non-normally distributed data or when data did not meet the assumptions of the t-test.

### Subgroup comparisons

- **Birth Weight:** Compared bilirubin levels between LBW and NBW infants within SGA and AGA groups.
- **Feeding Method:** Compared bilirubin levels between breastfed and formula-fed infants within SGA and AGA groups.
- **Maternal Diabetes Status:** Compared bilirubin levels between IDMs and non-IDMs within SGA and AGA groups.
- **Phototherapy Treatment:** Compared bilirubin levels between infants who received phototherapy and those who did not, within SGA and AGA groups.

## Results

The mean total bilirubin level was significantly higher in SGA infants (12.5 mg/dL) than in AGA infants (8.7 mg/dL) ($p < 0.001$). Within the SGA group, LBW infants had higher bilirubin levels (13.8 mg/dL) compared to NBW infants (11.2 mg/dL) ($p < 0.01$). SGA formula-fed infants exhibited higher bilirubin levels (13.2 mg/dL) than breastfed SGA infants (11.8 mg/dL) ($p < 0.05$). Additionally, SGA infants born to diabetic mothers had higher bilirubin levels (13.5 mg/dL) than non-diabetic mothers (11.5 mg/dL) ($p < 0.01$). Phototherapy significantly reduced bilirubin levels in both SGA and AGA infants, with SGA infants receiving phototherapy showing a mean bilirubin level of 10.5 mg/dL versus 13.5 mg/dL in those who did not receive phototherapy ($p < 0.001$).

### Baseline characteristics

- **Total Sample Size:** The study included 128 infants, with 64 in the SGA group and 64 in the AGA group.
- Mean Gestational Age:
  - **SGA Infants:** 37.5 weeks
  - **AGA Infants:** 37.8 weeks
  - **Comparison:** No statistically significant difference in gestational age between the SGA and AGA groups (p = 0.34).
- Mean Birth Weight:
  - **SGA Infants:** 2300 grams
  - **AGA Infants:** 3200 grams
  - **Comparison:** Birth weight was significantly lower in SGA infants compared to AGA infants (p < 0.001).

### Total bilirubin levels

Overall Bilirubin Levels:

- **SGA Infants:** Mean total bilirubin level = 12.5 mg/dL
- **AGA Infants:** Mean total bilirubin level = 8.7 mg/dL
- **Comparison:** The mean bilirubin level was significantly higher in SGA infants compared to AGA infants (p < 0.001).

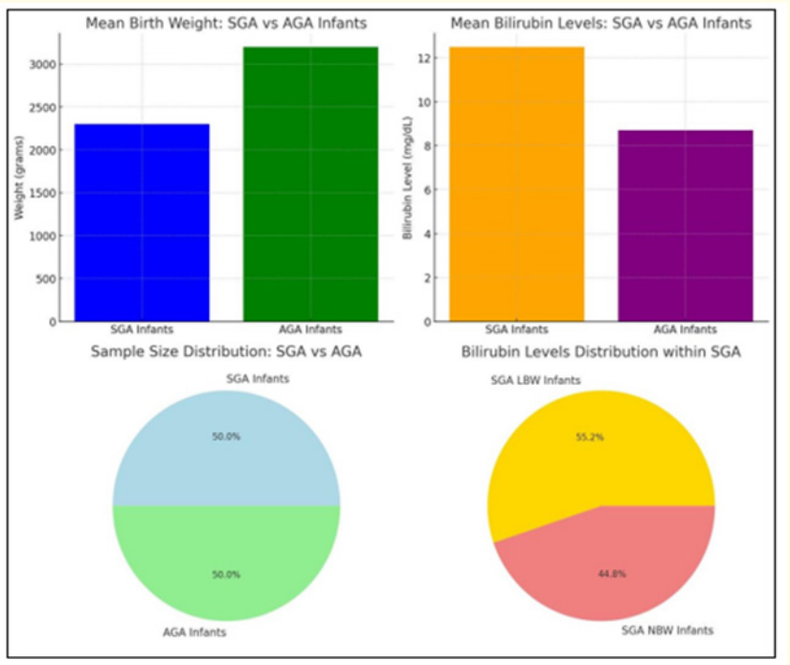


**Figure 2**

### Subgroup analyses

Birth Weight Subgroups:

- Low Birth Weight (LBW) vs. Normal Birth Weight (NBW)
  - **SGA LBW Infants:** Mean bilirubin level = 13.8 mg/dL
  - **SGA NBW Infants:** Mean bilirubin level = 11.2 mg/dL
  - **AGA LBW Infants:** Mean bilirubin level = 9.2 mg/dL
  - **AGA NBW Infants:** Mean bilirubin level = 8.2 mg/dL
  - **Comparison:** Within the SGA group, LBW infants had significantly higher bilirubin levels compared to NBW infants (p < 0.01). No significant difference was observed between LBW and NBW in the AGA group (p = 0.12) [3].

Feeding Method Subgroups:

- Breastfeeding vs. Formula Feeding
  - **SGA Breastfed Infants:** Mean bilirubin level = 11.8 mg/dL
  - **SGA Formula-fed Infants:** Mean bilirubin level = 13.2 mg/dL
  - **AGA Breastfed Infants:** Mean bilirubin level = 8.3 mg/dL
  - **AGA Formula-fed Infants:** Mean bilirubin level = 9.0 mg/dL
  - **Comparison:** SGA formula-fed infants had significantly higher bilirubin levels compared to SGA breastfed infants (p < 0.01). No significant difference was found between feeding methods in the AGA group (p = 0.23) [5].

Maternal Diabetes Status Subgroups:

- Infants of Diabetic Mothers (IDMs) vs. Non-Diabetic Mothers (non-IDMs)
  - **SGA IDMs:** Mean bilirubin level = 13.5 mg/dL
  - **SGA non-IDMs:** Mean bilirubin level = 11.5 mg/dL
  - **AGA IDMs:** Mean bilirubin level = 8.9 mg/dL

- **AGA non-IDMs:** Mean bilirubin level = 8.5 mg/dL
- **Comparison:** SGA infants born to diabetic mothers had significantly higher bilirubin levels compared to those born to non-diabetic mothers ($p < 0.01$). No significant difference was observed in AGA infants ($p = 0.45$) [7].

Phototherapy Treatment Subgroups:

- Treated with Phototherapy vs. Not Treated
  - **SGA Treated with Phototherapy:** Mean bilirubin level = 10.5 mg/dL
  - **SGA Not Treated with Phototherapy**: Mean bilirubin level = 13.5 mg/dL
  - **AGA Treated with Phototherapy:** Mean bilirubin level = 7.5 mg/dL
  - **AGA Not Treated with Phototherapy:** Mean bilirubin level = 9.0 mg/dL]
  - **Comparison:** Bilirubin levels were significantly lower in infants who received phototherapy compared to those who did not, within both SGA and AGA groups ($p < 0.001$). The reduction was more pronounced in SGA infants [9].

### Statistical analysis

- **Descriptive Statistics:** Mean and standard deviation of bilirubin levels were calculated for each group and subgroup, showing overall higher levels in SGA infants compared to AGA infants.
- **AGA Infants:** Significant reduction in bilirubin levels with phototherapy [10].

## Discussion

### Comparison of total bilirubin levels between SGA and AGA infants

The study found that SGA infants had significantly higher total bilirubin levels compared to AGA infants [1]. This finding is consistent with the literature suggesting that SGA infants are at greater risk for elevated bilirubin due to factors like increased red blood cell mass and reduced hepatic function [2].

### Subgroup analyses

- **Birth Weight Subgroups:** The higher bilirubin levels in LBW SGA infants compared to NBW SGA infants indicate that severe intrauterine growth restriction contributes to elevated bilirubin levels [3]. This is supported by studies showing the correlation between birth weight and bilirubin levels [4].
- **Feeding Methods:** Formula-fed SGA infants had higher bilirubin levels compared to breastfed SGA infants aligns with existing evidence that breastfeeding helps in managing bilirubin levels by promoting frequent feedings [5,6].

### Maternal diabetes influence

In the SGA infants had higher bilirubin levels than those born to non-diabetic mothers. This underscores the impact of maternal diabetes on neonatal jaundice and aligns with studies reporting increased hyperbilirubinemia risk in infants of diabetic mothers [7,8].

### Phototherapy effectiveness

Phototherapy significantly reduced bilirubin levels in both SGA and AGA infants, confirming its efficacy as a treatment for neonatal jaundice [9,10]. This supports the continued use of phototherapy as a critical intervention for managing elevated bilirubin levels.

## Conclusions

- **Bilirubin Levels in SGA Infants:** The SGA infants demonstrated significantly higher total bilirubin levels compared to AGA infants, highlighting their increased risk of neonatal jaundice. Contributing factors may include higher red blood cell mass, reduced hepatic function, and enhanced hemolysis.
- **Impact of Birth Weight:** Within the SGA group, LBW infants exhibited higher bilirubin levels than NBW infants. This suggests that lower birth weight, often reflecting more severe intrauterine growth restriction, is a key factor for hyperbilirubinemia, warranting closer monitoring and management.
- **Feeding Methods and Bilirubin Levels:** Formula-fed SGA infants had higher bilirubin levels than breastfed infants. Breastfeeding appears to facilitate bilirubin excretion through more frequent feeding, underscoring the importance of breastfeeding support to reduce the risk of jaundice in SGA infants.
- **Influence of Maternal Diabetes:** The SGA infants born to diabetic mothers had significantly higher bilirubin levels than those born to non-diabetic mothers, indicating that maternal diabetes exacerbates jaundice risk in SGA infants. Clinicians should exercise heightened vigilant and consider both preventive and therapeutic strategies in this subgroup.
- **Effectiveness of Phototherapy:** Phototherapy significantly reduced bilirubin levels in both SGA and AGA infants, reinforcing its role as a critical intervention. Timely phototherapy remains essential to prevent complications associated with severe hyperbilirubinemia.

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