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Assessment of Small for gestational age as a health risk for thyroid impairment in preterm infants

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Abstract

Background: Preterm birth occurs once a baby is born prior to actually 37 weeks of pregnancy. Small to gestation is typically described as being lower than tenth percentile from the indexed population's allocation of birth weights by gestation or being in the bottom 10% of birth weights. Being short to gestational age (SGA) was connected with a number of negative consequences, including decreased cognitive and sensorimotor function. The goal of the investigation was to confirm the idea that preterm SGA babies have greater TSH amounts and a greater prevalence of thyroid disease. Methods: This prospective cohort research included 80 preterm neonates from El-Bagour General Hospital's neonatal critical care unit. Preterm infants were separated into two groups: The study group consisted of 40 SGA preterm neonates, whereas the control group consisted of 40 AGA preterm newborns. Results: In the current study, the findings shown a substantial difference in TSH between the AGA preterm neonates group and the SGA preterm newborns group. SGA preterm neonates had considerably lower mean FT4 and FT3 values than AGA preterm newborns. According to our findings, there was a significant reduction in thyroid dysfunction among AGA preterm neonates compared to SGA preterm newborns. Conclusion: Thyroid dysfunction was more common in preterm SGA babies.

Keywords: Small to gestational age, thyroid dysfunction, risk factor, preterm newborns.

1. Introduction

Preterm birth is a significant issue in perinatal health care. Preterm delivery is a major risk factor for neurological disability, including cerebral palsy, and accounts for the majority of perinatal mortality. The expense of providing care for premature newborns that may spend many months in the hospital is growing. [1].

Prematurity is the greatest cause of newborn death and a major source of illness and impairment in children, accounting for up to half of all pediatric neurodevelopmental problems. [2].

Preterm birth occurs once a baby was born before the age of 37 weeks. [3]. The birth weight classifications are as follows: low birth weight (<2500 g), extremely low birth weight (<1500 g). birth weight (<1000 g) is quite low. [4].

Only roughly two-thirds of children with low birth weight are premature. Because they are tiny for their gestational age, term newborns may have low birth weight. These newborns are often described as falling below the 10th centile of the index population's distribution of birth weights by gestation, i.e., falling inside the bottom 10% of birth weights. [5].

Small for preterm delivery is typically described as being lower than the tenth percentile of the index population's allocation of birth weights by gestation, or being in the bottom 10% of birth weights.[4].

Being short to gestational age (SGA) connected with a number of negative consequences, including decreased cognitive and sensorimotor function. In accordance with a recent analysis, the majority of SGA births occur in poor and middle-income countries, with a concentration in South Asia, highlighting the need for effective measures to reduce disability, stunting, and non - modifiable illnesses. [6].

Thyroid hormones are required for proper central nervous system growth and maturation. Even temporary hypothyroxinemia in the first few weeks of infancy might lead to neurologic and mental complications later in life. Following the introduction of neonate screening (NBS) for congenital hypothyroidism (CH), L-T4 replacement treatment initiated during the first two weeks of life can restore thyroxine (T4) and TSH, preventing developmental impairments caused by late diagnosis. [7].

The hypothalamic-pituitary-adrenal axis and thyroid function may, at least in early life, control prenatal and postnatal development in SGA offspring [8]. TSH concentrations are much greater in preterm SGA babies, according to a recent study, and this should be considered when defining a reference interval for this population [9]. Furthermore, most SGA newborns will have catch-up growth (CUG) within young childhood, and CUG patterns are influenced by hypothyroidism and the use of L-T4 replacement medication[10].

Cianfarani et al. [11] reported increased TSH levels in children with SGA who have attenuated CUG, indicating that intrauterine reprogramming may include thyroid function, which may impact postnatal development. Because of the premature hypothalamic-pituitary-thyroid axis, preterm SGA babies are more prone to thyroid malfunction, such as temporary hypothyroidism and delayed TSH increase. [12].

The objective of this research was to confirm the hypothesis that preterm SGA babies have greater TSH levels and a greater prevalence of thyroid disease.

2.Patients and Methods

Subjects:

This prospective cohort research included 80 preterm neonates from El-Bagour General Hospital's neonatal critical care unit. Preterm infants were separated into two groups: The study group consisted of 40 SGA preterm neonates, whereas the control group consisted of 40 AGA preterm newborns.

Inclusion criteria: Preterm newborns (GA < 37 wk), including both SGA and AGA ones. SGA was described as a birth weight that was lower from the 10^{th} percentile to the particular GA and sex.

Exclusion criteria: Full term neonates. Admission after 1 week of age, death, loss to follow-up, maternal thyroid diseases and unavailable or incomplete records.

Every child was exposed to the following:

Full history taking included demographic characteristics included age, sex, BW, GA, being a twin, caesarean section delivery.

The history of conditions was collected, including 1- and 5-min Apgar scores, the presence of respiratory distress syndrome, intraventricular haemorrhage, necrotizing enterocolitis, and cardiac problems, as well as NICU procedures such as respiratory support (invasive or noninvasive), surfactant administration, and medication utilize (steroids, dopamine, and furosemide).

Examination

Investigations:

TSH, FT4 and FT3 assays.

The normal range references of hormone levels are presented as following: TSH (1.3 ~ 9.91 mU/L for male, 0.77 ~ 19.42 mU/L for female), FT4 (11.85 ~ 33.81 pmol/L), and FT3 (2.63 ~ 5.70 pmol/L) [(9)].

CH was defined as TSH > 40 mU/L in the initial TFT. Transient hypothyroidism was described as FT4 11.85 pmol/L and TSH 10 mU/L. Transient hypothyroxinemia was characterised as FT4 11.85 pmol/L and TSH 10 mU/L. (TH). TSH > 20 mU/L after a normal first TFT test was characterised as dTSH. Hyperthyrotropinemia is describe as FT4 11.85 pmol/L plus TSH 10 mU/L. Low T3 syndrome is identified as FT3 2.63 pmol/L with normal FT4 and TSH values. (**13**)..

Ethical consideration:

The study procedure was approved by Benha University's Ethical Scientific Committee. Before enrolling in the trial, parents provided informed permission and were fully informed about all study procedures.

Statistical analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science **(IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).** Data were given, and appropriate analysis was performed based on the data type gathered for each parameter.

Descriptive statistics:

1. Mean, Standard deviation (± SD) for parametric numerical data, while Median and range for non-parametric numerical data.
2. Frequency and percentage of non-numerical data.

Analytical statistics:

- **Student T** A test was employed to determine the statistical variance in means among the two research groups.
- **Chi-Square test** was used to examine the relationship with the two qualitative variables
- **r→Pearson's Product correlation coefficient:** it evaluates the linear association between 2 quantitative variables (one is the independent var. X, and the other is the dependent var., Y). value of "r" varies from -1 to 1

0= no linear correlation

1= perfect positive correlation

-1 = perfect negative correlation

Positive= increase in the independent variable leads to increase in the dependent variable

Negative = increase in the independent variable leads to decrease in the dependent variable.

P value was considered significant as the following:

* $P > 0.05$: Non significant

* $P \leq 0.05$: Significant

3.Results

We divided 80 preterm newborns into two groups: 40 SGA and 40 AGA, to establish the statistical variation in averages between the two research groups. In the context of demographic data, there's no important statistical variance between the AGA preterm neonates group and the SGA preterm newborns group (Table 1). There was neither large discrepancy in examination seen between AGA and the SGA preterm newborns group, however the AGA preterm newborns group exhibited an analysis of variance marked increase in 5-min Apgar scores (9.70.464) as matched to the SGA preterm neonates group (8.98.768).

In terms of TSH, there was a measurable difference between the AGA preterm neonates group and the SGA preterm newborns group. The mean FT4 and FT3 readings of AGA preterm babies were substantially greater than those of SGA preterm newborns (Table 2, and Fig. 1). There was a statistically significant reduction in thyroid dysfunction among AGA preterm neonates compared to SGA preterm newborns. Thyroid dysfunction was more common in the SGA preterm neonates group than in the AGA preterm newborns group (Table 2, Fig. 1,2).

TSH elevation was found to be significantly and a risk factor related to SGA (Table 3). Table 4 demonstrates that within the SGA preterm newborn group, It was no statistics correlation among gestational age and thyroid hormones. In the AGA preterm infant group, there had been no statistically important relationship between gestational age and thyroid hormones.

Table (1) Comparison between AGA preterm newborns group and SGA preterm newborns group regarding Demographic data.

			AGA preterm newborns group	SGA preterm newborns group	t.test	P. value
Age (days)	**Mean ± SD**		5.68± 1.54	5.78± 1.16	.327	.744
Sex	**Female**	**No.**	18	18	X^2	1.000
		%	45.0%	45.0%	.000	
	Male	**No.**	22	22		
		%	55.0%	55.0%		
BW (kg)	**Mean ± SD**		1.79± .474	1.49± 1.17	-1.489	.140
GA (weeks)	**Mean ± SD**		33.07± 2.14	33.72± 2.30	1.305	.196
being a twin	**no**	**No.**	34	27	X^2	.046
		%	85.0%	67.5%	3.382	
	yes	**No.**	6	13		
		%	15.0%	32.5%		
Caesarean section delivery	**CS**	**No.**	34	36	X^2	.499
		%	85.0%	90.0%	.457	
	NVD	**No.**	6	4		
		%	15.0%	10.0%		

Table (2) Comparison between AGA preterm newborns group and SGA preterm newborns group regarding investigations.

		AGA preterm newborns group	SGA preterm newborns group	t. test	P. value
TSH (uIU/mL)	**Mean ± SD**	6.06± 2.52	14.55± 47.80	1.122	.026
FT4 (pmol)	**Mean ± SD**	19.14± 5.84	15.73± 5.60	-2.660	.009
FT3 (pmol)	**Mean ± SD**	5.16± 1.22	4.42± .754	-3.237	.002

Table (3) Risk factors of TSH elevation in the study population.

		95% C.I. for EXP(B)		P. value
	Exp(B)	Lower	Upper	
TSH (uIU/mL)	1.964	.886	3.050	0.026

Table (4) Correlation between gestational age and thyroid hormones among (SGA preterm newborns group and AGA preterm newborns group).

Correlation	**SGA preterm newborns group**		**AGA preterm newborns group**	
	Pearson's correlation		**Pearson's correlation**	
	r	**r**	**p**	**p**
TSH (uIU/mL)	-.103-	.243	.131	.528
FT4 (pmol)	-.153-	.231	.151	.344
FT3 (pmol)	.062	.032	.847	.702

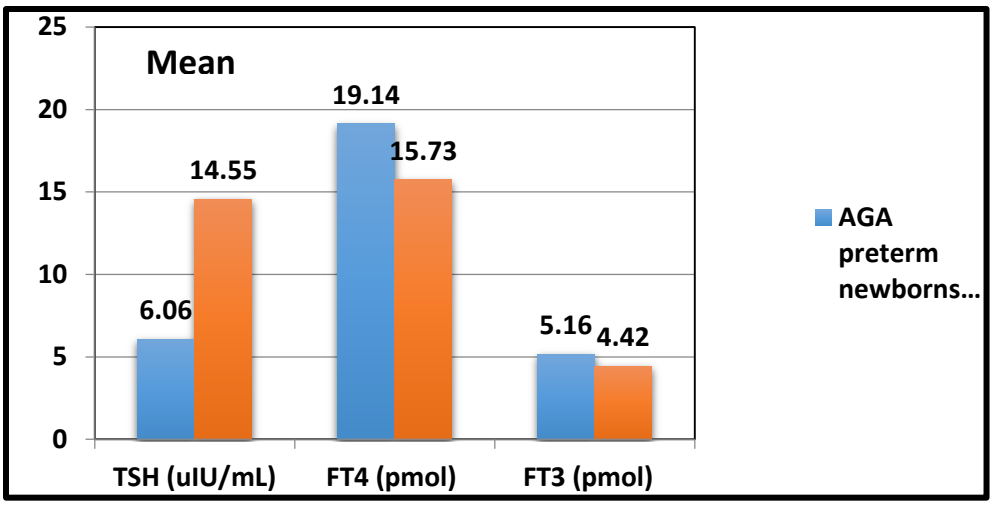

Fig. (1) shows a comparison among the AGA preterm babies group and the SGA preterm newborns group regarding investigations.

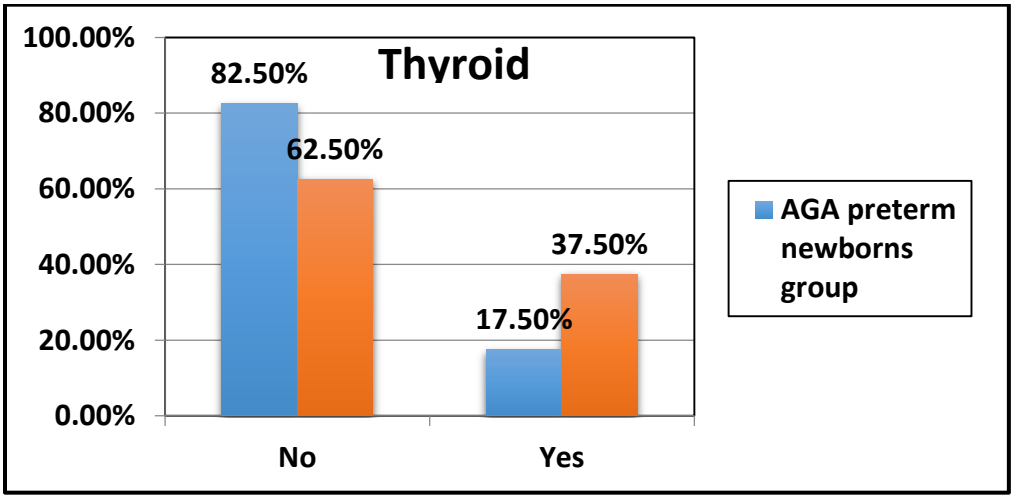

Fig. (2) shows a comparison between AGA preterm newborns group and SGA preterm newborns group in respect of thyroid dysfunction.

4. Discussion

In the present work, the results revealed a significant statistical distinction in TSH between the AGA preterm neonates' group and the SGA preterm newborns group. The mean levels of FT4 and FT3 were considerably lower in SGA preterm neonates than that in AGA preterm newborns. Our findings supported the findings of Liu et al. (13), who sought to validate the notion that preterm SGA babies have higher TSH values even inside the expected range and a greater incidence of thyroid disease. They discovered that the SGA group had considerably greater FT4 concentrations. According to Rai et al. [14], FT3 and FT4 levels were observed to be lower during severe illness.

Recent research has also discovered that SGA newborns who are at risk of thyroid dysfunction (TD) had considerably TSH values that be greater than with those of proper gestational age (13). Radetti et al. (15) discovered that TSH levels are much greater in SGA children, with 20% having TSH levels beyond the upper limit of the normal range, although no difference was seen for FT4. Children with preterm short SGA had greater TSH amounts that are normal range, although mean of FT4 is not statistically different, according to De Kort et al. (16).

The current study finds no significant difference in NICU procedures between both AGA preterm newborns group and the SGA preterm newborns group, but there was a statistically important correlation in intraventricular haemorrhage among the AGA preterm newborns group and even the SGA preterm newborns group. The usage of drugs such as insulin, furosemide, and vancomycin, as well as iodine exposure, have all been recognized as risk

factor in the development of dTSH [17]. This contradicts the findings of Lee et al. [18], who found that prenatal steroids were more common in AGA newborns than in SGA infants. Clinical severity indicators linked with the development of dTSH, including as respiratory distress syndrome, the use of a ventilator, and NICU hospitalisation, were less common in SGA infants. Lower Apgar scores, atrial septal abnormalities, and post-natal drug exposure were all equally common in the dTSH group as the non-dTSH group.

In terms of Low T3 syndrome, our study reported no significant variation seen between AGA preterm babies' group and the SGA preterm neonates group. Serum total T3 levels follow a trend similar to total T4, however they are proportionately lower in the majority preterm neonates, most likely due to the influence of NTIS (also known as the "low T3 syndrome") [19]. According to our findings, the AGA preterm neonates group showed a statistically significant lower degree of thyroid dysfunction than the SGA preterm newborns group.

Birthweight and SGA have been linked to thyroid dysfunction in extremely low birthweight (VLBW) neonates [20]. Thorpe-Beeston et al. [21] discovered that certain SGA fetuses had impaired thyroid function. Pregnant women with hyperthyroidism were more likely to experience fetal development limitation (22). He et al. [23] proposed that the key phase for maternal TSH and maternal FT4 is the first trimester for maternal TSH and the second trimester for maternal FT4. One possible explanation is that hyperthyroidism causes increased protein and lipid breakdown, resulting in prolonged caloric deficit and birth weight decrease [24].

Subclinical hypothyroidism has been linked to various negative pregnancy outcomes, including early birth and low birth weight [25, 26]. Cavarzere et al. [27] discovered a link between TSH and birth weight in newborns weighing 1,000 g. Hashemipour et al. [28] discovered that birth weight is substantially linked with thyroid function tests in a meta-analysis.

5. Conclusion

Preterm SGA neonate had a higher incidence of thyroid dysfunction. Thyroid function tests (TFTs) should be performed on SGA newborns on a regular basis.

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