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### RESEARCH PAPER

#### THE INFLUENCE OF THYROID HORMONES ON GAMMA IMMUNOGLOBULIN DENSITY (Ig-Gp) AND APGAR SCORE

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### ABSTRACT

Observations over the years, particularly in the labour rooms of Jos University Teaching Hospital (JUTH), and TANDAM Medical Centre, Jos, Plateau, Nigeria, indicates that several neonates respond differently to these parameters. However, the experience of four mothers who had protracted labour and neonates with weak cry and low muscle tone, prompted this present investigation. Ex-vivo placenta, maternal and cord blood of twenty deliveries (10 primipara and ten multipara; five of which were by elective caesarean section) were assayed for thyroid hormone in maternal serum and IgGp in maternal and cord sera; while the APGAR scores of the neonates were as well, documented. Results showed that the mean immunoglobulin G population (IgGp) or density of neonates compared with that of their euthyroid mothers though higher in neonates was not statistically significant ( $P > 0.05$ ). It was however significant ( $p < 0.01$ ) between neonates and their hypothyroid mothers. APGAR score of the neonates of the euthyroid mothers were higher ( $p < 0.05$ ) than those hypothyroid mothers who also bled for longer periods postpartum. It is our opinion that there could perhaps be an insight into the cause of such agonizing deliveries and to that effect, we recommended possible interventions.

**Key words:** *Euthyroidism, hypothyroidism, APGAR score, Gamma Immunoglobulin (IgG)*

### INTRODUCTION

Gamma immunoglobulin (IgG) represents the most abundant serum immunoglobulin (Ig) and has a role in mediating immunity. The human foetus receives a passive immunization by the selection passage of maternal IgG across the placenta (Gitlin et al., 1964). Other immune globulins are not transplacental and if detected in the foetal serum, they must be due to active synthesis by the foetus. IgG filtration begins around 12<sup>th</sup> week of gestation and the foetal serum IgG level increases as pregnancy advances (Gitlin and Biasucci, 1969, Yeung and Hobbs, 1968; Jones, 1969, Hyvarinen et al., 1973).

In an earlier report by Brambell et al. (1960), IgG is actively transported across the placenta and receptors plays an important role in this transfer. The active transport seems to be controlled by the maternal level of IgG which thus stabilizes the foetal IgG level (Gitlin, 1971). A review by Tatra and Placheta (1975) suggested on the contrary that all four IgG subgroups can cross freely the placenta barrier. However, the neonatal Fc receptor (FcRn) is a specific IgG transporter (Martre et al., 1975; Goldstein et al., 1988; Staurt et al., 1989; Micklem et al., 1990; Schmidt, 1989).

Of interest are the agonizing experiences of mothers who experience protracted labour and later give birth to neonates with weak cry and low muscle tone. Four such striking deliveries occurred at the labour rooms of Jos

University Teaching Hospital (JUTH) and TADAM Medical Centre, Jos, triggering this present investigation. We opined that perhaps, there could be an insight into these agonizing deliveries, upon which possible interventions can be recommended. Moreover, findings from an earlier laboratory work had implicated hypothyroidism with decreased muscle tone following decrease in serum  $Ca^{2+}$  concentration (Amadi et al 2007).

This study therefore, investigates the relationship between IgG density (IgGp) and muscle tone (a parameter in APGAR scoring) in both Eutyroid and Hypothyroid states. Other parameters in APGAR scoring or rating includes heart rate, activity (reflexes), Respiration, and Skin colour (see table 1).

**Table 1: APGAR Score Model**

Parameters	Scores		
	0	1	2
i. H~ Heart Rate	Nil	<100/m	>100/m
ii. A ~ Activity (Reflexes)	Nil	Grimance	Vigorous
iii. R~ Respiration	Nil	Weak cry	Strong cry
iv. M~ Muscle Tone	Limp	Slight	Active
v. C ~ Colour of Skin	White	Purple with Blue extremities	Pink all over
<b>Total</b>	<b>0</b>	<b>5</b>	<b>10</b>

## MATERIALS AND METHODS

**Study subjects:** Fifteen pregnant patients presenting at Jos University Teaching Hospital (JUTH) and five at TANDAM Medical Centre Jos were studied. Ten of the patients were primigravida, while ten were multigravida. Fifteen had vaginal delivery. Five of the women who turned out to be hypothyroid after screening (four at JUTH and one at TANDAM), had protracted labour and opted for elective Caesarean Section. Nevertheless, all the patients had normal after births.

**Ethical Clearance:** Ethical clearance was obtained from Jos University Teaching Hospital (JUTH), while informed consent was obtained from all the participants in this study.

**Study Population:** The study started with fifty pregnant mothers presenting at the JUTH ante-natal clinic but eventually, only twenty were selected based on the exclusion criteria.

**Inclusion Criteria:** Pregnant mothers with normal term pregnancy without any complication or infection of any kind were included in this study.

**Exclusion Criteria:** Pregnant mothers with spotting, pre-eclampsia, diabetes or any other type of disease/infection were excluded from the study.

**Sample/Data Collection:** Having obtained ethical clearance and informed consent of the patients, blood samples were taken from the antecubital vein of each mother and umbilical cord blood (mixed blood), within 1-5 minutes after the birth of the infant. The blood was allowed to clot at 18°C and the serum stored at 4°C.

APGAR score/rating, being a qualitative estimate of the condition of an infant 1 – 5 minutes post partum, was derived by assigning points (0, 1, and 2) to the quality of heart rate, respiratory effort/crying power, colour of the skin, muscle tone/reflexes and expressed as the sum of these points with the best score being 10.

**Sample Analysis:** IgGp was measured by immunohistochemical staining (immunohistochemistry) with anti- $FEA_1$ , and early endosomal marker. Human leucocyte endothelial cells (HULEC – 5A) cells (mononuclear cells) which had been pulsed with Alexa 647 –labelled  $H_{435}$  A, were stained with this marker which tags to neonatal constant fraction receptor (FcRn) or IgG receptors since IgG is primarily seen in early endosomes (Sedmak et al 1991) and then chased for 20 minutes. Thus, IgGp in both maternal and cord sera was estimated. All the immunostains were monoclonal antibodies (British Drug House, Poole, England). The thyroid hormone level in each mother's serum was estimated by the method of Lee (1964), as specified by WHO International Laboratories (Kits) for Biological Standards, London (Courtesy of TANDAM Medical Centre). The mean value of thyroid hormone (T4) was recorded for euthyroid and hypothyroid groups as the assays portrayed.

**Statistics:** The data collected were statistically analyzed using ANOVA (SPSS version 17) to assess the contribution of thyroid hormones in IgG population and APGAR score.

**RESULTS**

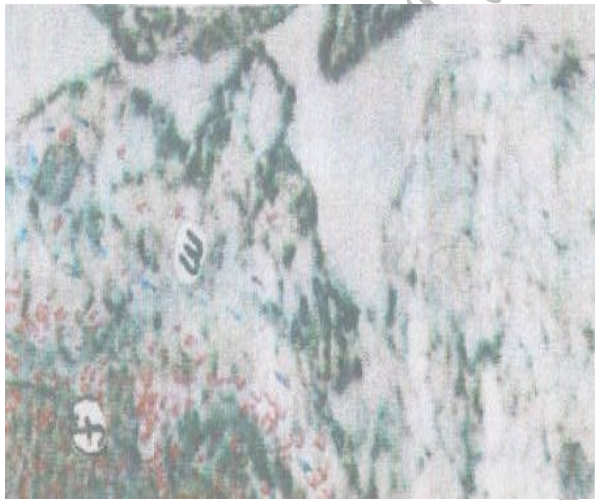
The results of Mean and Standard Error of Mean (SEM) and IgG Density (IgGp) of mothers and neonates as well as the mean T<sub>4</sub> levels of the mothers and APGAR scores of neonates are displayed in tables 2 and plates 1, 2 and 3.

Plate 1 shows a longitudinal section of umbilical cord and ex-vivo term placenta of euthyroid mother. IgG (reddish patches) are more on foetal side (f) than maternal side (m) showing vectorial mobility. Plate 2 is a transverse section of ex-vivo, term placenta of hypothyroid mother showing IgG as fluorescent white spots distributed more or less evenly on both maternal end (m) and foetal side (f) displaying scalar mobility. Plate 3 is a transverse section of ex-vivo, term placenta showing part of the vasculature (v) surrounding a central mucous area (m).

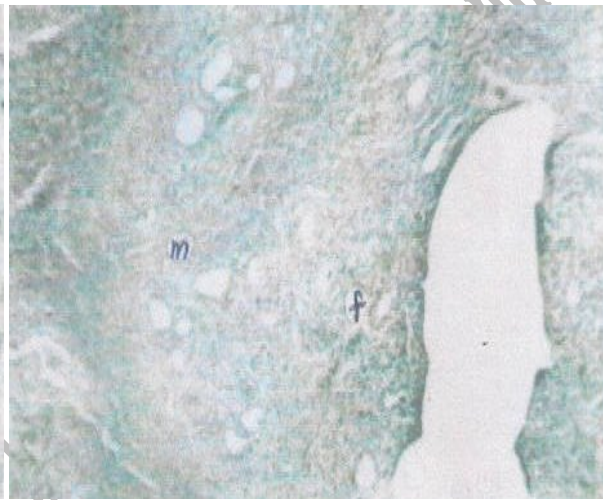
**Table 2: Comparative IgG density, Apgar score, and thyroid hormone levels in neonates of hypothyroid and euthyroid mother**

	IgG Density in mothers		IgG Density in neonates		APGAR score		Maternal serum T4 (ng/Dl)	
	HM	EM	HM	EM	HM	EM	HM	EM
	0.25	11.0	2.5	10.0	7	10	0.6	3.8
	0.50	10.50	3.0	11.5	8	7	0.6	4.0
	0.30	11.50	2.0	12.0	6	10	0.5	3.5
	0.25	10.0	2.5	10.5	7	8	0.8	3.0
	0.25	10.0	2.5	11.0	7	10	0.5	2.8
<b>X±SEM</b>	<b>0.76±0.44</b>	<b>10.70±0.35</b>	<b>2.5±</b>	<b>11.0±0.05</b>			<b>0.6±0.05</b>	<b>3.45±0.05</b>

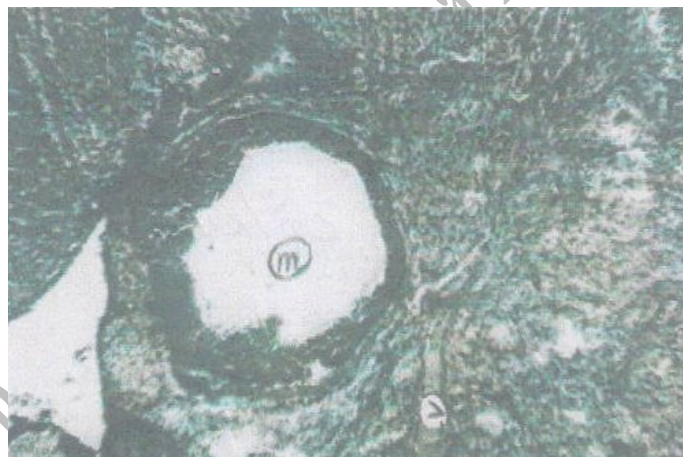
**Key:** HM= Hypothyroid Mothers, EM= Euthyroid mother, T4=Thyroid hormone Levels.



**Plate 1:** Longitudinal section of umbilical cord and ex-vivo term placenta of euthyroid mother x4000. Showing vectorial mobility of IgG (reddish patches) more on foetal side (f) than maternal side (m).



**Plate 2.** Transverse section of ex-vivo term placenta of hypothyroid mother x4000. Showing scalar mobility of IgG (Fluorescent with sport) distributed more or less evenly on both maternal end (M) and foetal side (f)



**Plate 3.** Transverse section of term placenta x4000. Showing part of vasculature (v) surrounding a central mucous area (m)

## DISCUSSION

In the current study ex-vivo term placenta, maternal and cord blood have been used to analyze the materno-foetal transfer of IgG by determining the IgGp in maternal and cord blood by tagging the antibody with fluorescent dye and comparing the population with APGAR scores of the neonates. Our finding was that the IgGp increased in umbilical cord blood in euthyroid women but a sharp decline ( $p < 0.01$ ) in hypothyroid mothers irrespective of mode of delivery, barring complications. It was however noted that the hypothyroid mothers had protracted dystocia lasting eight to ten hours. Some five mothers (25%) were in labour for periods that precipitated Caesarean section.

Euthyroid mothers had their babies per vaginal within two to four hours. On the other hand hypothyroid mothers had very slow cervical dilatation suggesting hypothyroidism as a factor affecting duration of labour and the level of IgG in cord blood. These findings appear reasonable since it is generally assumed that the pressure of the uterine contraction during parturition leads to filtration of IgG into the foetal circulation (Payne, 1969; Cochran, 1972; Turmero, 1974). The strong uterine contractions in euthyroid mothers probably enhanced IgG filtration into the cord circulation; but the weak contractions of hypothyroid myometrium would not filter much IgG across the materno-foetal circulation.

Hypothyroidism has been reported earlier to cause feeble contraction (Tata, 1964); consequent on severe myotonia (Adeniyi et al., 1994; Amadi et al., 1999; 2007). Thyroid hormone is known to switch on  $Ca^{2+}$  receptors for vigorous concentrations (Amadi et al., 2007). The findings in the present investigation might justify our suggestion that thyroid hormone screening be incorporated into ante-natal clinics to spare hypothyroid pregnant women of protracted labour and postpartum haemorrhage. Moreover, it directly mirrors the pregnancy outcome with respect to the quality of life of the neonate.

Much as the resistance to the passage of the neonate through the birth canal filters IgG into the foetal circulation (Payne 1969; Cochran 1972; Turmero 1974), the thyroid hormone level of the mother appears an obvious natural determinant of the neonatal passive immunization (IgGp) and its APGAR score. Our results strongly suggest that hypothyroidism factors into the decreased IgGp of the neonate and the corresponding low APGAR score. That is to say that the thyroid hormone status of the mother appears to directly correlate with the materno-foetal IgG transfer and the APGAR score of the neonate. Thus, thyroid hormone screening during antenatal care is recommended for the future of maternal cum neonatal health.

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#### **AUTHOR(S) CONTRIBUTION**

All authors took part in the data collection, collation, data analysis and report writing.