



ASN-PH-020919  
ISSN: 2315-5388

**International Journal of Basic, Applied and Innovative Research**

**IJB AIR, 2013, 2(2): 32 - 36**

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## RESEARCH PAPER

### **THE RELATIONSHIP OF GAMMA IMMUNOGLOBIN (IgG) DENSITY AND APGAR SCORE IN NORMAL TERM PREGNANCY**

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Received: 21<sup>st</sup> May, 2013

Accepted: 7<sup>th</sup> July, 2013

Published: 31<sup>st</sup> July, 2013

## ABSTRACT

The transfer of maternal IgG provides the neonate with humoral immunity during early life. The population of transferred IgG or IgG density (IgG<sub>p</sub>) was estimated to find out if it has any relevance to the condition of an infant 1-5 minutes after birth or APGAR score which gives an insight into the state of health of the infant and thus its chances of survival and its milestone of development. Ex-vivo, term placenta of forty euthyroid mothers, the maternal serum, and cord blood were used to estimate the IgG<sub>p</sub> in both maternal and cord blood by taking blood samples from the antecubital vein of the mother and from the umbilical cord (mixed blood) immediately after birth; having determined the APGAR score within 1-5 minutes post-partum. The findings featured the following: the mean APGAR score (10); mean IgG<sub>p</sub> of the neonates ( $11.94 \pm 0.12\text{mg}/100\text{ml}$  of blood); mean IgG<sub>p</sub> of the maternal blood ( $10.9 \pm 0.29/100\text{ml}$ ). The difference however, was not statistically significant ( $P > 0.05$ ). The findings provide evidence suggesting that IgG<sub>p</sub>, not only relates to, but determines APGAR score of the neonates.

**Keywords:** APGAR score, IgG density, Term placenta, Cord blood

## INTRODUCTION

Gamma immunoglobulin (IgG) is actively transported across the placenta and the constant fraction (Fc) of Immunoglobulin fragment is reported to play an important role (Brambell et al., 1960). Thus, the human foetus receives a passive immunization by the selective passage across the placenta of maternal IgG (Gitlin et al., 1968). There are reports that filtration of IgG begins around the 12<sup>th</sup> week of pregnancy (Gitlin and Blascucci, 1969) and the foetal serum level increases as pregnancy advances (Young and Hobbs, 1968; Jones, 1969; Hyrinen, et al., 1973).

Expression of this Fc receptor is not only restricted to the pre-or neonatal period, when it plays a role in the delivery of maternal IgG to offspring (Rocewald and Abrahamson, 1982; Story et al., 1994); but can also be ubiquitously found in endothelial cells of adult tissues where it is believed to be involved in IgG homeostasis (Duncan, et al., 1995; Kristofferson, 1996).

Some IgG are however, synthesized by the foetus itself; approximately 1-5% of the total IgG in the umbilical cord blood being of foetal origin (Fundenberg and Funderberg, 1964; Martenson and Fendenberg, 1965). In this regard the present investigation made use of ex vivo placenta model which has implicated neonatal constant fraction receptor (FcRn) in the delivery of IgG across the materno-foetal barrier such that FcRn is an IgG transporter.

## MATERIAL AND METHODS

**Subjects and Study Population:** The study covered 40 patients who had a vaginal delivery (10 primigravida and 30 multi-gravida).

All the pregnancies were normal. The neonates were also healthy and their weights were more than 2.5kg. They had no complications during their stay at the maternity hospital and all the mothers had normal after births.

**Ethical Considerations:** Ethical clearance and informed consent of the patients were obtained to carry on the study.

**Inclusion and Exclusion Criteria:** Only mothers that attended regular antenatal clinics and carried the pregnancy to term without complications were included in the study. Patients with any form of illness including toxemia of pregnancy, were excluded from the study.

**Data Collection:** Immediately after vaginal delivery, the concentration of IgG in the maternal serum and the umbilical cord blood were measured as well as the APGAR scores of a neonate. The relationship between these parameters was then established.

Blood samples were taken from the antecubital vein of the mother and from the umbilical cord (mixed blood) immediately after birth of the infant. The trafficking of IgG was investigated by the modified method of Daniel et al., (1991); by immunohisto chemical staining with anti FEAL (Sandoz, Basel, Switzerland) which is an early endosomal marker that pulses the IgG. By means of immunofluorescence imaging (following the IgG by the fluorescence of the tagged fluorescence dye) the fate or migration of IgG following pinocytotic uptake into endothelial cells chases for 20 minutes.

Furthermore, fluorescense dye was injected into ex-vivo placenta artery and the umbilical cord within 2-3 minutes of expulsion. Microvasculature derived cells (with the aid of a dissecting microscope) were used in preference to endothelial cells isolated from large vessels since FcRn is preferably expressed in micro-vessels (Daniel et al., 1991).

All pulse-chase experiments were carried out at 37°C in a medium depleted of serum IgG (BDH chemicals Ltd. Poole, England) at pH 7.0. Pulsing at this pH precluded the possibility that IgG binds to cell surface FcRn prior to uptake, as FcRn- IgG interaction is not permissive at near neutral pH (Matre et al., 1975). The corresponding APGAR score was recorded as shown in Table 1 Model.

**Table 1: APGAR Score Model**

	Parameters	0	1	2
i	H-Heart rate	nil	< 100/min	>100/min
ii	A-Activity (Reflexes)	nil	Grimance	Vigorous
iii	R- Respiration	nil	Weak cry	Strong cry
iv	M-Muscle Tone	Limp	Slight	Active
v	B-Colour	White	Purple with blue extremities	Pink all over

**Statistical Analysis:** The data obtained were statistically compared with control by means of student-t-test.

## RESULTS

The mean IgGp in 30 mothers as shown in Table 2 was 10.9 ±0.29mg/100ml while that of the neonates was 11.94 ± 0.12 with APGAR score 10. The neonates' IgGp was higher than that of the mothers.

In Table 3 however, representing 10 patients, shows the mean IgGp (11.0) for the mother and 10.70 for the neonates with APGAR score of 7. The IgGp of neonates, though higher than the patients' in each case, was not statistically significant (P>0.05). The lower IgGp of neonates in Table 3 compared to table 2, recorded a correspondingly lower APGAR score of 7, compared to 10 in Table 2. The APGAR score was statistically significant (P<0.05) in the two groups, notwithstanding the non-significant status of IgGp (P>0.05).

**Table 2: Mean IgG population (Density) mg/100ml of serum in Mother and Child (Multigravida).**

	<b>Mothers</b>	<b>Neonates</b>	<b>APGAR Rating</b>
(n=6) for each value	11.0	12.0	2
	10.5	11.5	2
	11.5	12.0	2
	10.0	12.2	2
	11.5	12.0	2
	X=10.9 ±0.29	11.94 ± 0.12	10 Total

Mother c/f Neonatal IgGp: P>0.05ns

**Table 3: IgG Population (Density) mg/100ml of blood in Mother and Child (Primigravida)**

	<b>Mothers</b>	<b>Neonates</b>	<b>APGAR Rating</b>
(n=2) for each value	10.0	1.0	2
	11.5	10.5	1
	12.5	11.0	2
	10.0	10.2	1
	11.5	10.0	1
	X=11.0 ±0.0	10.70±0.0	7 Total

Mother c/f Neonatal IgGp: P>0.05ns

## **DISCUSSION**

In the current study, we have used ex-vivo placental assay to investigate a possible role of FcRn in mediating transfer of IgGp across the human placenta. The results indicate that FcRn is a pre-requisite for an antibody to cross the maternofetal barrier. This provides direct evidence to support the role of FcRn in the transcytosis of IgGp across the human placenta, and is consistent with the observation that FcRn is expressed in placenta syncytiotrophoblast (Story et al., 1994; Kristoferson and Natre, 1996; Leach et al., 1996; Sinister et al., 1996).

The results also showed that there was a wide range of IgGp levels in the umbilical cord blood. This probably, may be due to the methodology or perhaps, the mode of delivery that might influence umbilical cord serum IgGp levels. Our observations showed that umbilical cord IgGp level was higher than that of the mother but this was not statistically different (P>0.05).

It had earlier been reported that IgGp levels in the umbilical cord blood of the newborn, appears to be significantly higher after vaginal delivery (Yang et al. 1968). The difference could be due to the mechanical effect of traversing the birth canal. This differs with uterine contractile force and duration of labour, all of which might influence the IgGp level of the new born. However, there is a contrary assumption by Hyvarinen et al., (1973), that uterine activity does not play a role on IgGp level in the newborn.

We would like to insist however, that the pressure of uterine contractions in labour leads to filtration of IgGp into the foetal circulation and this agrees with the assertion by Payne, (1969); Cochran, (1972); Turmero, (1974). Most importantly, the present observations are justified by the APGAR scores that correlated positively with IgGp status of the neonates (both in primipara and multipara). As such, we opine that in a normal vaginal delivery, following an uncomplicated pregnancy, there exists a positive relationship between IgGp density and APGAR score in a normal term placenta.

## **ACKNOWLEDGEMENT**

Our gratitude goes to Dr. O. G. Douglas of Lagos, Island Maternity Hospital, Jos University Teaching Hospital, and Prof. JAM Otubu (TADAM Medical Centre Jos) for their indispensable help in sample collection and analysis.

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## **AUTHORS CONTRIBUTION**

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