

Amudalat Issa
Mohammed B Abdulkadir
Omotayo O Adesiyun
Bilkis Owolabi
Surajudeen O Bello
Ruqayat R Bakare

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Serum brain natriuretic peptide in healthy Nigerian newborn babies

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Amudalat Issa (✉)
 Children Specialist Hospital, Ilorin,
 Nigeria
 Email:
 issahamdallah27@gmail.com

Mohammed B Abdulkadir
 Omotayo O Adesiyun
 Ruqayat R Bakare
 Department of Paediatrics and
 Child Health, University of Ilorin
 Teaching Hospital / University of
 Ilorin, Nigeria.

Bilkis Owolabi
 General Hospital, Ilorin, Nigeria.

Surajudeen O Bello
 Dalhatu Araf Specialist Hospital,
 Lafia Nasarawa State.

Abstract: *Background:* Brain natriuretic peptide (BNP) is a sensitive biomarker that is valuable in the management of childhood heart failure. Studies have reported racial differences in the level of BNP, especially in the adult population. The level of BNP in healthy Nigerian newborn babies is unknown. Hence, we determined the level of BNP in healthy term appropriate for gestational age (AGA) newborn babies.

Methods: This was a cross-sectional study, 85 healthy term AGA newborn babies aged 24 to 72 hours. The babies had relevant demographic parameters documented in a proforma and BNP assay analysed using ELISA method.

Results: The median IQR serum BNP level was 341.43 (313.39 to 425.45) pg/ml. The median level in females, was higher than males, {393.86 (296.97- 460.62) pg/ml vs 328.05 (313.61-389.39) pg/ml, $p > 0.05$ }. There was no significant relationship between serum BNP and birth weight, chronological age, gestational age, or mode of delivery ($p > 0.05$ in each case).

Conclusion: The study demonstrated high BNP levels in healthy term Nigerian newborns. There was no relationship between BNP, the chronological age, birth weight, gender, gestational age or mode of delivery in babies between 24 to 72 hours of life.

Keywords: Brain natriuretic peptide, term babies, healthy, Nigeria.

Introduction

Natriuretic peptides are ring-shaped amino acid sequences that serve important biochemical functions in animals. Three types have been described in humans namely A, B and C.¹ Atrial natriuretic peptide (ANP) is synthesized and released from the right atrium. It has vasodilatory, diuretic and natriuretic properties.¹ Brain natriuretic peptide (BNP) was first discovered in porcine brains.² However, BNP has been found to be highly concentrated in the ventricles of the heart, hence, the current name B-type natriuretic peptide. C-type natriuretic peptide is found in the brain and coronary vessels.³

Brain natriuretic peptide is a 32 amino acid polypeptide containing a 17 amino acid ring structure common to all natriuretic peptides.² BNP is produced and released from the membrane granules of the myocardium in response to pressure and volume overload.⁴ Pro-BNP, the inactive precursor is cleaved into active BNP following the release from the myocardial granules. The inactive precursor has a half-life of 60 minutes while the active BNP has a half-life of about 20 minutes.⁴ These biomarkers peak in the first 3 to 4 days after birth and fall rapidly throughout the first month to low levels in childhood.⁵ BNP is known to cause diuresis, natriuresis, vasodilatation and antagonizes renin-angiotensin-aldosterone system leading to a reduction in intravascular volume, ven-

tricular preload, and afterload.⁵ It is excreted largely by the kidneys, though endocytosis and lysosomal degradation also play a role.⁶ Other cardiac biomarkers in clinical practice are markers of necrosis (creatinine kinase, cardiac troponins, heart-type fatty acid binding protein); and inflammatory markers (C reactive protein). The most reliable of these biomarkers are cardiac troponins and brain natriuretic peptide.⁷

Authors have documented distribution of BNP in healthy children ranging from first day of life up to 18 years.^{8,9,10} These studies demonstrated age to be a determinant of serum BNP level in healthy children.^{8,9,10} The studies demonstrated highest BNP in the first four days of life due to hemodynamic changes at birth.¹⁰ Most of the studies reported no relationship between serum BNP level and gender while a single study reported significantly higher level in female older than 10 years. Brain natriuretic peptide being a sensitive and reliable marker in the assessment and management of heart disease in children has gained popularity over the years. Despite its increasing popularity and relevance in clinical practice, a literature search revealed no published study on BNP levels among healthy African newborn babies. This study was therefore, designed to document BNP levels in healthy term Nigerian newborns.

Materials and Methods

This descriptive cross-sectional study involving 85 newborn babies was conducted in the postnatal wards of the University of Ilorin Teaching Hospital between January and March 2017. Ethical clearance was obtained from the Hospital Ethics Review Committee. Written informed consent was obtained from parents after a clear explanation of the study objectives.

Inclusion criteria were term appropriate for gestational age (AGA) healthy newborns. The babies were recruited between 24 to 72 hours of life. Babies with clinical suspicion of congenital heart disease, major congenital anomalies, history of risk for sepsis, and clinical suspicion of sepsis were excluded. All the babies had their anthropometric parameters recorded and were classified based on gestational age using Lubchenco chart.¹¹ Two millilitres of blood were collected from a convenient peripheral vein and transferred into a plain bottle. The blood sample was allowed to clot and fully retract for two hours at room temperature, then centrifuged at 1000 rpm for 15 minutes; serum was harvested and stored at -80°C in the Chemical Pathology laboratory.

The serum BNP was analyzed using human brain natriuretic peptide, BNP ELISA kit by Elabscience. The kit allows for in vitro quantitative determination of human BNP concentration in serum, plasma, and other body fluids. The ELISA kit uses the principle of competitive enzyme immunoassay and comes with a microplate well that is pre-coated with an antigen specific to human BNP (Elabscience manual). Analysis of BNP was done after samples had been collected from all subjects.

Data obtained was entered into a computer and analyzed using Statistical Package for Social Sciences (SPSS) software version 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Mean and median were generated for continuous variables. Tests of relationship (Mann-Whitney U, Kruskal Wallis) and association (Spearman's correlation) were computed as appropriate. The results were presented using tables. A p value of less than 0.05 was considered statistically significant.

Results

Eighty-five healthy AGA newborn babies were recruited between 24 to 72 hours of life with mean \pm SD age of 31.47 ± 17.13 hours. The subjects comprised 44 (51.8%) females, and 41 (48.2%) males. The mean \pm SD gestational age was 39.12 ± 1.45 weeks (Table 1). Majority (71.8%) of the babies were spontaneous vertex deliveries. The mean \pm SD birth weight was 3.08 ± 0.32 Kg as shown in Table 1

Table 1: General characteristics of the study population

Variable	Mean \pm SD
Age at sample collection (hours)	31.5 \pm 17.1
Gestational Age (weeks)	39.1 \pm 1.5
Birth weight (Kg)	3.1 \pm 0.3
Occipitofrontal circumference (cm)	34.5 \pm 1.5
Length (cm)	48.8 \pm 2.7
Sex	n (%)
Male	44 (51.8)
Female	41 (48.2)
Mode of delivery	
Spontaneous vertex	61 (71.8)
Emergency Caesarean section	12 (14.1)
Elective Caesarean section	10 (11.8)
Assisted vaginal	2 (2.4)

Figures in brackets are percentages of the study population

The median (IQR) serum BNP was 341.43 (313.39 to 425.45) pg/ml. The serum level in females, 393.86 (296.97-460.62) pg/ml, was higher compared to that of male subjects, 328.05 (313.61-389.39) pg/ml but the difference was not significant, $p = 0.153$. Similarly, the levels were comparable across chronological age, gestational age groups, birth weight and delivery categories ($p > 0.05$ in each), Table 2.

Table 2: Serum BNP levels across gender, gestational age and postnatal age in the participants

Variable	Serum BNP Median (IQR) (pg/ml)	U/ K	p
Sex			
Male	328.05 (313.61 - 389.39)	739.500	0.153
Female	393.86 (296.97 - 460.62)		
Chronological age s			
24 - <48 hours	339.49 (311.64 - 418.24)	432.000	0.283
48 - 72 hours	389.39 (322.47 - 604.61)		
Birth weight (g)			
2500 - 3000	341.43 (313.61 - 422.16)	887.50	0.912
3001 - 3999	339.49 (306.30 - 441.55)		
Mode of delivery			
SVD	339.45 (313.39 - 415.84)	598.00	0.340
CS	369.36 (315.84 - 500.90)		
Gestational age group			
37 - 38 weeks	335.63 (296.97 - 414.06)	0.650	0.723
39 - 40 weeks	340.46 (314.06 - 434.07)		
41 - 42 weeks	397.84 (314.45 - 503.34)		

U: Mann-Whitney U test, K: Kruskal-Wallis test. BNP: Brain natriuretic peptide

SVD: Spontaneous vertex delivery, CS: Caesarean section

Linear correlation showed no significant association between serum BNP and selected characteristics of the general population (age, gender, birth weight, gestational age and mode of delivery), $p > 0.05$ in all, as shown in Table 3.

Table 3: Correlation of serum BNP with general characteristic of the population

Variables	Serum BNP	
	R	p
Chronological age	0.068	0.538
Sex	0.156	0.154
Birthweight	0.067	0.540
Mode of delivery	-0.104	0.343
Gestational age	0.065	0.557

Discussion

Brain natriuretic peptides is increasingly being deployed in diagnosis, monitoring and prognosticating heart disease in the paediatric population.^{10,12} Despite its increasing popularity and relevance in clinical practice, a literature search revealed no published study on BNP levels among healthy African new born babies.

The current study reported median (IQR) serum BNP levels of 341.43 (313.39 to 425.45) pg/ml in healthy babies. This is higher than mean \pm SD of 231.60 \pm 197.50 to 278.98 \pm 190.47 pg/ml in previous studies among healthy Caucasian neonates.^{13,14} Differing statistical analysis methods may limit strict comparison as the current study reported median (IQR) while the earlier one reported mean \pm SD of serum BNP. It is also higher than median (IQR) of 242.00 (152.20 to 343.50) pg/ml reported among healthy Italian neonates.¹⁵ The higher values herein reported may be attributable to racial differences. This is in keeping with earlier studies which demonstrated 1.5 fold higher values among Black adults

in comparison with Caucasians.¹⁶

The lack of relationship between serum BNP, gender and gestational age in healthy term neonates is consistent with other studies.^{9,15} The finding of no association between serum BNP, gender, gestational age and birth weight and mode of delivery could not be compared because previous studies did not correlate serum BNP with these parameters.

Considering the difference between the serum BNP level in the current study compared with other studies and documented racial variation in adult population,¹⁶ it will be attractive to conduct a large population study among African neonates to confirm normal BNP levels in the neonates and compare with their Caucasian counterpart. The limitations in the current study include relatively small study population, narrow age range of recruitment, single rather than serial assay which limits comparison and generation of reference values.

Conclusion

The study demonstrated high BNP levels in healthy term Nigerian newborns compared with Caucasian counterpart in the first 24 hours to 72 hours of life. There was no relationship between the chronological age, birth weight, gender, gestational age and mode of delivery among the newborns in the first 24 to 72 hours of life.

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