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Socio-economic and Socio-demographic Determinants of BNP values in children with Pneumonia In Benin City

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RESEARCH

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ABSTRACT

Background

The level of BNP is usually used as a guide to heart failure. However, there is need for the level of this peptide to be known in non-cardiac conditions that may cause inflammation and hypoxia.

Aims

To determine socio-demographic determinants of BNP in children with pneumonia. To determine the socio-economic determinants of BNP in children with pneumonia.

Methods

Over a year, consecutive children diagnosed radiologically with pneumonia were evaluated echocardiographically for CHD. Also, children with heart failure were excluded. Inclusion criteria included all those children with ongoing pneumonia without any evidence of any other co-morbidity whether acute or chronic. Biodata and sociodemographic variables of children with pneumonia that met the inclusion criteria were collected and studied.

Results

Of the 50 subjects recruited for the study, 26 (52 per cent) were males. The mean age for males 14.27±13.33, females 12.03±11.83, mean height for males 74.00±3.46 and 72.00±0.00 for females, the mean weight range from 8.30±1.87 and 7.08±3.40 for males and females respectively. The mean BNP value for all subjects was 459.55±422.61, of which males had a mean value of 500.33±.399.93 and females 415.38±450.25 with a p value of 0.483. The mean brain natriuretic factor for weight range 1–5.9kg was 203.83±116.04 that of 6–10.9kg was 645.22±314.26, while that of 11–15.9kg was the lowest with 115.85±72.46.

Conclusion

Apart from congenital heart disease and several other morbidities both chronic and acute, sociodemographic characteristics of the patient and some clinical features may also affect BNP levels in the blood. Patients with pneumonia had higher mean values of BNP when compared with normal cut-off.

Key Words

Brain natriuretic peptide, children, pneumonia

What this study adds:

1. What is known about this subject?

BNP is known to be elevated in subjects with cardiac morbidities especially heart failure, it is important in the diagnosis of heart failure in children.

2. What new information is offered in this study?

From our study, we now know that other factors other than cardiac morbidity may affect the level of BNP in children.

3. What are the implications for research, policy, or practice?

In terms of practice and research, one would have to recognise these socio-economic and socio-demographic factors as co-founding variables.

Background

Brain natriuretic factor or peptide or B-type natriuretic factor (BNP) or natriuretic peptide B is a 32-amino acid polypeptide secreted by the ventricles of the heart in response to excessive stretching of heart muscles cells or cardiomyocytes.[1] The physiological action of BNP is similar to those of atrial natriuretic peptide and includes a decrease in systemic vascular resistance, increased natriuresis, reduced blood pressure.

The diagnosis of heart failure remains essentially clinical based on history, physical examination, and chest radiograph findings. However, clinical findings and examination alone are often inadequate in diagnosing heart failure as multiple other conditions that affect the cardiopulmonary system mimic the symptoms of heart failure. This confounds the diagnosis and delays the initiation of appropriate management. In this setting, the existence of a biomarker that could accurately identify heart failure as the cause of patient's symptoms would be extremely helpful in guiding timely initiation of appropriate management. Natriuretic peptides, namely BNP and NT-proBNP, present themselves as such markers and are now being widely used in diagnosing and managing heart failure.[2]

In a study in the United States for instance, we already know that children with heart disease have high BNP levels above 200pg/ml, while normal children had below 100pg/ml. This index study will enable us know whether children with non-cardiac pathology still have values below 100pg/ml. More importantly the factors affecting the levels of BNP will determine the adequacy of these single cut-offs. Although not clearly stated in the study cited above, children with values ranging from 100–200pg/ml are likely to have non-cardiac inflammatory pathology.

Apart from identifying those with heart problems especially those with CHD,[3] the levels of BNP among those with CHD varies significantly higher in those with functional heart muscle problems like congestive cardiac failure.[4] Therefore, children with cardiac and non-cardiac pathology that may have developed CCF even from cases as simples as fluid overload are also frequently identified by the BNP.

Apart from studying the diagnostic impart of ANP in the evaluation of cardiac disease, the study of the blood levels of BNP may find usefulness in other childhood conditions that may affect the heart.

In line with the above Kawamura and co-worker[3] studied blood levels of BNP as a useful biochemical marker for myocarditis in patients with Kawasaki disease.[3] Clinically, this will provide a very useful, easy and reliable way of detecting cardiac involvement in many of the paediatric primarily non-cardiac cases.

A more critical look at the above may have necessitated the study of BNP in predicting the severity of community acquired pneumonia. In a study by Li et al.,[4] it was found that BNP level is positively correlated with the severity of CAP, and may be used as a biomarker for evaluating the severity of CAP. The increase in BNP level in patients with cap may be due to BNP secretion in response to tissue hypoxia which may lead to pulmonary vasoconstriction, pulmonary hypertension and right ventricular overload. Generally, pneumonia is a hypoxic condition in the pulmonary circulation and in the general circulation.[4] Based on these findings, it is therefore hypothesised that the severity of CAP and the increased BNP level were mainly due to inflammatory response and local hypoxia in the pulmonary circulation.[4] Therefore, predicting the severity of CAP will help and enable the clinician to proactively put in place facilities and the required manpower to address the problems of severe pneumonia which is a major killer of children.[4] This will help reduce the mortality and improve the outcome of the cases of the very common killer of children in the tropics.[4]

A recent study[5] found that inflammatory response can cause the release of BNP and that BNP levels and CRP values are significantly correlated. Other studies also show that 1L-1b, 1L-6, TNFα and other proinflammatory cytokines can induce BNP secretion from cardiomyocytes cultured in virto.[6,7]

Similarly, bacterial endotoxin was found to directly increase the expression of BNP mRNA in the myocardial cells of rat.[8] In adults, the effect of age, sex and other factors like menstrual cycle has been properly studied.[9] This has not been clearly done in children. Considering the relevance of the levels of BNP in diagnosing and identifying those with heart problem, it is imperative to know what the levels are in other children without cardiac problems. This prompted the authors of the current study to evaluate the levels of BNP in non-cardiac patient in Nigeria. In this study the socioeconomic and sociodemographic determinants of the levels of BNP were carefully evaluated to expose possible relationship between the BNP and the named above factors. As previously studied by other workers, if indeed such relationships exist, cut-offs will be based on the

socioeconomic or demographic parameters instead of a single cut-off.

Method

Consecutive patients presenting to the children's emergency room of the University of Benin Teaching Hospital (UBTH) with pneumonia between March 2014 and February 2015, were recruited for the study. A chest radiograph was done for each patient as part of the routine investigation for pneumonia in the centre. The radiograph was read by the radiologist and the paediatric pulmonologist (WOO). Pneumonia was confirmed when both reports were positive. All the cases of pneumonia underwent transthoracic 2 Dimensional (2D) and Doppler echocardiography, done by the paediatric cardiologist (WES). Any congenital heart disease so found was excluded from the study. Children with heart failure were also excluded. The biodata, anthropometry and other sociodemographic parameters were documented. They included age, gender, socioeconomic class (SEC), weight and height. The SEC was determined using the method described by Olusanya et al.[10] Laboratory and clinical parameters of these patients like PCV, WBC, SPO2, duration of admission and outcome of admission were documented at presentation, during admission and at discharge. The information was obtained with the aid of a proforma. Ethical approval was given by the Ethics Committee of the UBTH.

Heart failure was diagnosed when the patient fulfilled the clinical diagnostic criteria of heart failure outlined below.[11]

1. Significant tachycardia for age (>160 beats/min in infancy, >140/min at 2 years, >120/min at 4 years and >100/min above 6 years.) Where fever was present, a 10/ min for every 1°C rise in temperature was allowed for.
2. Significant tachypnea for age(>60 cycles/min in the newborn, >40 cycles/ min <24 months, 30 cycles/ min in 2–5 years, >28 cycles/ min in 5–10 years and >25 cycles/ min in >10 years).
3. Cardiomegaly(displaced apex beat with a central trachea or cardiothoracic ratio >60 per cent in <5 years and >50 per cent in >5 years).
4. Tender hepatomegaly of at least 3cm size below the right costal margin.

The fulfilment of at least three of the four criteria above was diagnostic of congestive heart failure. The diagnosis of heart failure was made by a senior registrar or a consultant. And such patients with pneumonia but diagnosed to have heart failure were also excluded from the study. In this study, pneumonia was diagnosed by a combination of history, examination findings and radiological features. Patients presenting with fever, cough and difficulty with breathing by the informant were selected, examination findings revealing presence of fever, child been tachypnic and dyspnic and in some cases presence of crepitations in the lungs. Diagnosis was confirmed by a consultant paediatric pulmonologist (OOW) based on the presence of consolidation on chest x-rays of the patients. The patients with pneumonia were treated with antibiotics.

Statistical analysis

The data were coded and entered into and analysed using SPSS 16 (Chicago IL). Age, sex and socio-economic class were represented in percentage; weight, height BNP levels were presented in means ± standard deviation. The level of significance was set at $p<0.05$ and determined using χ^2.

Results

Fifty subjects were recruited for this study. Of the 50, 26 (52 per cent) were males and 24 (48 per cent) females. Of this number, 12 belong to the high socio-economic class, 20 belong to the middle and 18 to the lower socio-economic class. The mean BNP level for all subject was 459.55±422.61, males had a mean BNP value of 500.33±399.93, while females had a mean BNP value of 415.38±450.25 (Tables 1-4).

Discussion

The mean value of BNP children with complicated pneumonia in this study is 459.55±422.61. This value is higher than cut-offs recommended for patients without pneumonia from other studies. In a study from the United States of America, values for normal children were set at below a 100pg/ml.[4] This shows that children with pneumonia have higher values when compared with healthy children. This agrees with the study of Li et al.[4] who found that the level of BNP is positively correlated with severity of CAP.[4] Although in this study, the pneumonia severity index was not calculated for each patient and correlated with the value of the BNP, in the index study the pneumonia severity index could not be calculated due to unavailable data. The outcome (discharged or died) and the duration of stay in the hospital was used in the current study to determine severity.

The values of BNP were found to be lowest in those that spent the least number of days on admission. For instance, those that spent up to 10 days had mean values of 708.26±341.66. However, after the 10 day, the mean BNP value started diminishing. This may be due to fact that those

that stayed above 10 days may not stay due to severity but may stay for other reasons, for instance, in our environment, due to financial reasons or otherwise. When the outcome was considered, those that were discharged had lower values compared to those that died. If the duration of stay is a reflection of severity of pneumonia, just like the outcome, where those that died are more likely to have severe illness, then the more severe cases of pneumonia in the index study had higher values although the difference was not statistically significant (p=0.815).

In the index study, certain socioeconomic parameters were found to influence the distribution of the BNP levels. For instance, males had higher values than females (500.33±399.33 *vs.* 415.38±450.25). Younger children (infants) also had higher values than older children. Those aged 0–12 months had a mean BNP value of 533.40±446.96 compared to 37–48 months with a value of 135.30±0.00, p=0.289. This compares favourably with findings from studies done by other workers in different areas.[9,12,13] In the same vein, when the socioeconomic status of the subjects were considered, there was a positive correlation between the mean BNP value and the socioeconomic status, with those in the low socioeconomic status having a higher value than those in the higher class. There is no clear reason for this socio-economic class except that those in lower socio-economic class are more likely to live in hypoxic environment and may also be malnourished with low haematocrit which can possibly lead to higher BNP. Weight significantly affected the distribution of the mean BNP values, with the heavier children having lower values.

Furthermore, some clinical parameters like the PCV, WBC and SPO2 also affected the distribution of BNP values in children with pneumonia in the index study. In terms of the WBC which is also a reflection of severity of the pneumonia children with WBC <10,000 had a mean BNP value of 126.73±66.76 and those >10,000 had 894.17±433.41 with a p value of 0.000. When SPO2 was considered, SPO2 of ≤94 per cent had very highly elevated mean BNP values, while values of SPO2 like ≥95 per cent and above had lower values. These are similar to findings by other workers on BNP in other areas.[3,4] The reason for this is thought to be the effect of hypoxia on the heart which leads to stimulation of the BNP. However, the PCV does not agree with findings by other workers,[3,4] they demonstrated an inverse relationship between the PCV and BNP, that type of relationship was not found in this study. Therefore, it is important to note that when considering the use of BNP values in children with cardiac conditions and those with pneumonia, it is important to realise and recognise the fact that certain factors are closely related to the distribution of the BNP value in these category of children and if this is not considered properly, the diagnostic importance of such values may not be realised. In terms of cut off points, it is relevant to have separate cut off points for males and females. There may be need to also consider separate cut off points depending on certain clinical parameters.

Conclusion

The distribution of BNP value in children which is already known to be elevated in children with heart disease is affected and related to certain patient-related, socio-demographic and clinical parameters. Children with pneumonia also have elevated values.

References

1. Maher KO. B-type natriuretic peptide in the non-cardiac pediatric patient. Emory University Children's Healthcare of Atlanta, Atlanta Georgia, United States, 2006. Retrieved from https://clinicaltrials.gov/ct2/show/NCT00330811
2. Elsharawy S, Hassan B, Morsy S, et al. Diagnostic value of N-terminal pro-brain natriuretic peptide levels in pediatric patients with ventricular septal defect. The Egyptian Heart Journal. 2012;64(4):241–246.
3. Kawamura T, Wago M. Brain natriuretic peptide can be a useful biochemical marker for myocarditis in patients with Kawasaki disease. Cardiol Young. 2002;12:153–8.
4. Li J, Ye H, Zhao L. B-type natriuretic peptide in predicting the severity of community-acquired pneumonia. World J Emerg Med. 2015;6(2):131–136.
5. Shor R, Rozenman Y, Bolshinsky A, et al. BNP in septic patients without systolic myocardial dysfunction. Eur J Intern Med. 2006;17:536–540.
6. Weinfeld MS, Chertow GM, Stevenson LW. Aggravated renal dysfunction during intensive therapy for advanced chronic heart failure. Am Heart J. 1999;138:285–290.
7. Ma KK, Ogawa T, de Bold AJ. Selective upregulation of cardiac brain natriuretic peptide at the transcriptional and translational levels by pro-inflammatory cytokines and by conditioned medium derived from mixed lymphocyte reactions via p38 MAP kinase. J Mol Cell Cardiol. 2004;36:505–513.
8. Tomaru Ki K, Arai M, Yokoyama T, et al. Transcriptional activation of the BNP gene by lipopolysaccharide is mediated through GATA elements in neonatal rat cardiac myocytes. J Mol Cell Cardiol. 2002;34:649–659.
9. Clark BA, Elahi D, Epstein FH. The influence of gender, age, and the menstrual cycle on plasma atrial natriuretic peptide. J Clin Endocrinol Metab. 1990;70:349–52.
10. Olusanya O, Okpere E, Ezimokhai M. The importance of

socioeconomic class in voluntary fertility control in a developing country. W Afr J Med. 1985;4:205–212.
11. Omokhodion SI. Childhood heart failure. In: Omokhodion SI, Osinusi K, editors. Pediatric cardiology and respiratology. WACP update series. Lagos, Nigeria: West African College of Physicians. 1996:72–82.
12. Redfield MM, Rodeheffer RJ, Jacobsen SJ, et al. Plasma brain natriuretic peptide concentration: impact of age and gender. J Am Coll Cardiol. 2002;40:976–82.
13. Danser AH, Derkx FH, Schalekamp MA, et al. Determinants of inter-individual variation of renin and prorenin concentrations: evidence of a sexual dimorphism of (pro)renin levels in humans. J Hypertens. 1998;16:853–62.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

Ethical approval has been granted: ADM/E 22/a/VOL. VII/910.

Table 1: Socio-demographic characteristics of study population

Demographic	Male	Female	p-value
Sex	26 (52%)	24 (48%)	
Mean Age (months)	14.27±13.33	12.03±11.83	0.892
Mean Height (cm)	74.00±3.46	72.00±0.00	
Mean Weight (kg)	8.30±1.87	7.08±3.40	0.014
Socioeconomic status			
1 High Class	4 (33.33%)	8 (66.67%)	
2 Middle Class	12 (60.00%)	8 (40.00%)	
3 Low Class	10 (55.55%)	8 (44.45%)	

Table 2: Socioeconomic status with Brain natriuretic factor

Demographic characteristics		Mean	Percentage	Standard deviation	P-value
Sex	Male	26	52		
	Female	24	48		
Mean Age (months)	Male	14.27	52	13.33	0.535
	Female	12.03	48	11.83	
	All subjects	13.2	100	12.56	
Mean Height (cm)	Male	74	66.67	3.46	0.484
	Female	72	33.33	0	
	All subjects	73.33	100	2.88	
Mean Weight (kg)	Male	8.3	45.45	1.87	0.325
	Female	7.08	54.55	3.4	
	All subjects	7.64	100	2.82	
Socioeconomic status	1 High Class	1.67	24	0.49	0
	2 Middle Class	3	40	0	
	3 Low Class	4.33	36	0.49	
	Total	3.16	100	1.09	

Table 3: The BNP Levels by some socio-demographic and socioeconomic status of children with pneumonia

Demographic Parameters		BNP Values		
		Mean values	Standard Deviation	p-value
Sex	Male	500.33	399.93	0.483
	Female	415.38	450.25	
	Total	459.55	422.61	
Age	0-12 months	533.4	446.96	0.289
	13-24 months	282.9	291.96	
	25-36 months	384.7	420.27	
	37-48 months	135.3	0	
	Total	459.55	422.61	
Weight	0-5.9kg	203.83	116.04	0.000**
	6-10.9kg	645.22	314.26	
	11-15.9kg	115.85	72.46	
	Total	388.46	325.73	
Socioeconomic status	High Class	217.27	160.46	0.07
	Middle Class	521.68	395.17	
	Low Class	552.04	36	
	Total	459.55	422.61	

** Highly significant at α level 0.01.

Table 4: Natriuretic Factor and Clinical/Laboratory Parameters of Subject

Clinical Parameters		BNP Values		
		Mean values	Standard Deviation	p-value
PCV	10 – 20	0	0	0.025
	21 – 30	331	301.17	
	31 – 40	516.65	433.73	
	41 – 50	1137	0	
	Total	485.14	416.82	
WBC	<10,000	126.73	66.76	0.000**
	>10,000	894.17	433.41	
	Total	455.63	479.56	
SPO2	≤ 94%	2143.3	107.48	0.000**
	≥ 95%	617.03	46.15	
	Total	510.82	474.25	
Duration of Admission	1 – 5 days	375.73	387.87	0.186
	6 – 10 days	708.26	341.66	
	11 – 15 days	684	785.2	
	≥ 16 days	462.95	452.7	
	Total	539.87	440.32	
Outcome	Discharged	476.43	422.1	0.815
	Died	547.55	67.53	
	Total	479.27	414.63	

**Highly significant at α level 0.01.