

**BIOCHEMICAL PARAMETERS OF UMBILICAL
CORD BLOOD IN NIGER DELTA, NIGERIA:
TOWARDS ENSURING EFFICIENT CORD BLOOD
STEM CELL TRANSPLANTATION.**

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20 **ABSTRACT:**

21 **Aim:** The aim of this study was to determine the levels of basic biochemical parameters like uric
22 acid, potassium, sodium, bicarbonate and chloride in umbilical cord blood with a view to assess
23 its suitability for stem cell transplantation.

24 **Study Design:** This is a cross-sectional prospective study.

25 **Place and duration of the study:** The study was carried out at the Departments of Obstetrics
26 and Gynaecology, and Chemical Pathology University of Benin Teaching Hospital, Benin City
27 Nigeria between July 2010 and March 2011.

28 **Methodology:** Cord blood from a total of 164 pregnant women (HIV, hepatitis B and C
29 negative) who delivered in University of Benin Teaching Hospital from July 2010 to March 2011
30 were analyzed for some basic biochemical parameters.

31 **Results:** The levels of the biochemical parameters were sodium 135.4 ± 6.1 mmol/L (128 to
32 150 mmol/L), potassium 7.08 ± 1.9 mmol/L (4.5 to 14.7 mmol/L), bicarbonate 19.6 ± 2.4 mmol/L (14-
33 25 mmol/L), chloride 101.7 ± 3.8 mmol/L (90-109 mmol/L) and uric acid 1.63 ± 0.9 mmol/L (0.19-
34 3.09 mmol/L). chloride was the most stable with a CV of 3.71% while uric acid was the least
35 stable with a CV of 12.63%.

36 **Conclusion:** Umbilical cord blood could become an important source of stem cell in sub-sahara
37 Africa especially with the large number of deliveries. However careful selection of quality cord
38 blood must be enforced to avoid contaminants and haemolysis which may be responsible for
39 the hyperkalaemia as seen in this study.

40

41 **Key words:** Haematopoietic Stem cells, umbilical cord blood, biochemical parameters,
42 hyperkalaemia

43

44 INTRODUCTION

45 Cord blood has been shown to be a source of stem cells for transplantation. The first cord blood
46 transplantation was performed for a 5year old child with fanconi's anaemia, by Dr. Gluckman
47 and colleagues in October 1988¹. Also the first cord blood transplant for haemoglobinopathy
48 was in 1995 by Issaragris et al². As at 2007, at least 350,000 to 400,000 Umbilical cord blood
49 (UCB) units have been banked with over 6000 UCB transplant performed worldwide.³ UCB has
50 become a fully established source of stem cell for transplanting malignant and non malignant
51 disorders with reduced incidence of graft versus host disease.^{4,5}

52 Cord blood mononuclear cells are comprised of a heterogenous population of haematopoietic
53 and mesenchymal stem cell, endothelial progenitor cells and immature immunological cells^{6,7}.
54 The conventional medical use of cord blood is limited to haematopoietic reconstitution⁸, with
55 clinical trials ongoing in type 1 diabetes mellitus⁹, and cerebral palsy¹⁰.

56 Preclinical studies have demonstrated efficacy of cord blood in diverse conditions ranging from
57 heat stroke,^{11,12} to amyotrophic lateral sclerosis¹³, to post infarct regeneration¹⁴, to liver failure.¹⁵

58 In haematopoietic stem cell transplants ablation of recipient marrow is required to eradicate the
59 endogenous stem cell compartment, and HLA matching with post transplant immune support is
60 used to prevent graft versus host disease (GVHD)⁸. For non-haematopoietic applications such
61 as cardiovascular or neurological indications, the therapeutic activities of the cord blood are
62 believed to be mediated in many cases by growth factor secretion.^{16,17}

63 Tumor lysis syndrome describes the metabolic complications of either rapid tumor cell turnover
64 or chemotherapy induced tumor cell lysis. The syndrome is characterized by hyperuricaemia,
65 hyperphosphataemia, hypocalcaemia, hyperkalaemia and acute renal failure^{18,19}. The acute
66 renal failure is associated with large increase in plasma uric acid level. The pathophysiology of
67 uric acid nephropathy includes intratubular precipitation of uric acid causing mechanical

68 obstruction, direct toxicity to epithelial and endothelial cells and potential activation of the innate
69 immune system^{20,21,22}. Occasionally, patients will develop tumor lysis syndrome spontaneously,
70 but the majority of cases are associated with chemotherapy before the widespread adoption of
71 prophylaxis, most cases of acute renal failure in tumor lysis syndrome were due to uric acid
72 nephropathy²⁴.

73 Since chemotherapy is a very important process in stem cell transplantation especially in
74 ensuring marrow ablation, which can result to tumor lysis syndrome and its complications such
75 as electrolyte derangement. In this study, we analyzed some biochemical parameters of cord
76 blood as a way of ensuring the quality of cord blood collected for stem cell transplantation in
77 order to minimize post transplant complications that may arise from derangement of these
78 analytes.

79 **PATIENTS AND METHOD:**

80 Cord blood from a total of 164 HIV, hepatitis B and C negative pregnant women who delivered
81 in University Of Benin Teaching Hospital, Benin City, Nigeria between July 2010 and March
82 2011 were collected. The pregnant women were properly briefed about the study and informed
83 consents were obtained from them before umbilical cord blood was collected, 4.5mL of the
84 umbilical cord blood was collected in a 5mL specimen collection tube containing 0.5mL lithium
85 heparin as anticoagulant; this was in keeping with blood to anticoagulant ratio of 9:1. After
86 collection, the tube was immediately inverted 8-10times to ensure adequate anticoagulation of
87 the specimen. The specimens were centrifuged for 5minutes at 3,000rpm. The plasma were
88 separated into clean covered plain tubes and stored in an ultrafridzer at -80⁰c within 30minutes
89 of collection.

90 The plasma sodium, potassium, bicarbonate and chloride were analyzed using the ion selective
91 electrode system (ISE 4000) while the uric acid was analyzed using uricase method.

92

93 **STATISTICAL ANALYSIS:**

94 Statistical package for scientific solutions (SPSS), version 16 was used for the statistical
95 analysis. All values were reported as mean ± standard error of mean (SEM).

96 **RESULTS:**

97 The levels of the biochemical parameters were; sodium 135.4 ± 6.1 mmol/L (128 - 159 mmol/L),
98 potassium 7.08 ± 1.9 mmol/L (4.5 - 14.7), bicarbonate 19.6 ± 2.4 mmol/L (14 - 25 mmol/L),
99 chloride 101.7 ± 3.8 mmol/L (90 - 109 mmol/L) and uric acid 1.63 ± 0.9 mmol/L (0.19 - 3.09
100 mmol/L) (Table 1). Chloride was the most stable of all the analytes with a coefficient of
101 variation (C V) of 3.71%, followed by sodium with a CV of 4.49%. uric acid was the least stable
102 analyte with a coefficient of variation of 12.63% (Table 2).

103 There was a significant positive correlation between sodium and chloride with a p-value of 0.01
104 ($r=0.362$), sodium and bicarbonate with a *P-value of 0.002*. There was a positive correlation
105 between sodium and uric acid ($r=0.121$) bicarbonate and chloride ($r=0.165$) bicarbonate
106 and uric acid ($r=0.063$) chloride and but the correlation was not significant with a *P-value* greater
107 than 0.05. However, there was a negative correlation between sodium and potassium ($r=-0.37$)
108 potassium and bicarbonate, ($r=-0.045$) potassium and chloride, ($r=-0.0146$) potassium and uric
109 acid ($r=-0.163$) but the correlation was not significant with a *P-value* greater than 0.05 (Table 3).

110 Figure 1 is a histogram showing plasma potassium level in umbilical cord blood compared with
111 the high normal reference value in the University of Benin Teaching Hospital.

112 **DISCUSSION:**

113 In this study, we demonstrated that umbilical cord blood has low normal sodium level and
114 hyperkalaemia, although results from previous studies reported high levels of aldosterone in
115 neonates²⁵ compared to their mothers²⁶, aldosterone has been previously shown to cross the
116 placental barrier from the mother to the foetus²⁷ and highest aldosterone levels detected in cord
117 blood are consistent with de novo synthesis in the fetal adrenal gland given the very early
118 expression of the aldosterone synthase gene starting from the 13 gestational weeks²⁸. The
119 reason for the low normal sodium and hyperkalaemia could be the result of the inability of the
120 fetal kidneys to appropriately control sodium and water reabsorption as a result of the impaired
121 ability of nephronic segments to adequately respond to aldosterone action. The neonatal weight
122 loss related to extracellular fluid loss²⁹, which occurs during the first week after birth, is likely to
123 be the consequence of this tubular insensitivity. Yet, the physiological trigger and the role of this
124 transient sodium and water negative balance in newborn infants are still unclear.

125 From a pathophysiological perspective, it has been reported that plasma aldosterone levels and
126 potassium concentration levels are higher in low birth weight infant³⁰, similarly, preterm infants
127 have higher aldosterone levels and hyperkalaemia than full term infants^{31,32}. Given that low
128 birth weight infants have greater risk of developing adult hypertension³³, high levels of plasma
129 aldosterone and hyperkalaemia may thus serve as important biochemical parameters and
130 represent risk factors for dysregulated renin-angiotensin aldosterone system and early onset of
131 a high blood pressure. It is very likely that neonatal insensitivity to aldosterone action varies with
132 birth weight and could be a predictive factor of future chronic disease with a possible
133 involvement of gene development programming as recently described for glucocorticoids
134 sensitivity³⁴.

135 The umbilical cord blood bicarbonate level was low normal which is in agreement with previous
136 studies that defined fetal metabolic acidaemia as an umbilical vessels pH of less than 7.20 and
137 base excess of less than -8.^{35,36} The uric acid and chloride levels were within normal range.³⁷

138 Considering the fact that most of the patients for stem cell transplantation are prone to
139 developing tumor lysis syndrome either as a result of rapid tumor cell turnover or chemotherapy.
140 The syndrome is characterized by hyperuricaemia, hyperphosphataemia, hypocalcaemia and
141 acute renal failure^{18,19}. The acute renal failure is associated with large increase in plasma uric
142 acid level. The pathophysiology of uric acid nephropathy includes intratubular precipitation of
143 uric acid causing mechanical obstruction, direct toxicity to epithelial and endothelial cells, and
144 potential activation of the innate immune system^{20,21,22}. There is every need to ensure that the
145 umbilical cord is devoid of any form of electrolyte and uric acid derangement.

146 Umbilical cord blood could become an important source of stem cell in sub-sahara Africa
147 especially with the large number of deliveries, Shahrokri S. et al in Iran highlighted the
148 importance of umbilical cord blood stem cell transplantation as a potential cure for blood
149 diseases³⁸. However, careful selection of quality cord blood must be enforced, avoiding
150 haemolysis which may be partly responsible for the hyperkalaemia as noted in this study in
151 order to minimize post transplant complications that may arise from derangement of these
152 biochemical analytes.

153 **ACKNOWLEDGEMENT:**

154 We wish to thank Mr. Paul Aikorie of Chemical Pathology Department, UBTH, for helping us
155 out with some of the biochemical analysis.

156 **Competing Interest:** Apart from non availability of equipment/reagents to carryout immune-
157 genetic analysis of the samples which would have extend the scope of this study, no other
158 competing interest exist.

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159 **Authors' contributions:** There was equal contribution of all the authors to this study. All the
160 authors read and approved the final manuscript.

161 **Consent:** The pregnant women were properly briefed about the study and an informed consent
162 was obtained from them before the umbilical cord blood was collected.

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TABLE 1: THE LEVELS OF THE VARIOUS BIOCHEMICAL PARAMETERS IN CORD BLOOD

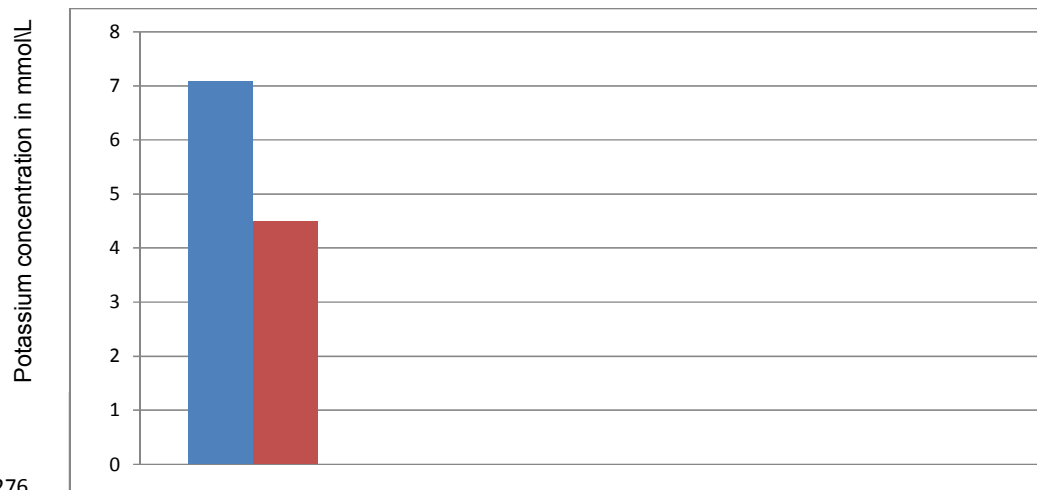
Biochemical Analyte	Minimum (mmol/L)	Maximum (mmol/L)	Mean (mmol/L)	Standard Deviation
Na+	128	150	135.44	6.088
K	4.5	14.7	7.08	1.875
HCO	14	25	19.60	2.356
Cl	90	109	101.74	3.773
Uric acid	0.19	3.09	1.63	0.857

TABLE 2: COEFFICIENT OF VARIATION OF THE VARIOUS BIOCHEMICAL PARAMETERS

Biochemical Analyte	Coefficient of Variation (%)	comment
Na+	4.49	
K	6.48	
HCO	5.02	
Cl	3.71	Most stable measurement
Uric acid	12.63	Least stable measurement

TABLE 3: CORRELATION STUDIES FOR THE VARIOUS ANALYTES

association	Correlation (r)	P-value	comment
Na vs K	0.37	.80	No sig. correlation
Na vs HCO	0.42	.002	Sig. correlation
Na vs Cl	0.362	.01	Sig. correlation
Na vs Uric acid	0.121	.40	No sig. correlation
k vs HCO	0.045	.76	No sig. correlation
K vs Cl	0.146	.31	No sig. correlation
K vs Uric acid	0.163	.26	No sig. correlation
HCO vs Cl	0.165	.25	No sig. correlation
K vs Uric acid	0.063	.66	No sig. correlation
Cl vs Uric acid	0.035	.81	No sig. correlation



276

277 **Figure 1**

278 This is a histogram showing plasma potassium levels in umbilical cord blood Vs high normal
279 reference value in the University of Benin Teaching Hospital.

280

281 Key:

282

283  Umbilical cord blood

284

285  High normal reference value in the University of Benin Teaching Hospital

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