

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

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21 **ABSTRACT:**

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

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

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

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

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

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

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43 **Key words:** Haematopoietic Stem cells, umbilical cord blood, biochemical parameters,

44 hyperkalaemia

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47 INTRODUCTION

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

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

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

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

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

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

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

82

83 **PATIENTS AND METHOD:**

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

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

96

97 **STATISTICAL ANALYSIS:**

98 Statistical package for scientific solutions (SPSS), version 16 was used for the statistical
99 analysis. All values were reported as mean $\pm$ standard error of mean (SEM).

100

101 **RESULTS:**

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

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

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

117

118 **DISCUSSION:**

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

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

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

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

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

159 **ACKNOWLEDGEMENT:**

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

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

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

167 **Consent:** The pregnant women were properly briefed about the study and an informed consent
168 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

284

Potassium concentration in mmol/L



285

286 **Figure 1**

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

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290 Key:

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Umbilical cord blood

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High normal reference value in the University of Benin Teaching Hospital

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