Research Article

Comparative analysis of cardio metabolic profile before and after 34 weeks in Ghanaian preeclamptic patients

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Abstract

Background: Over the past decade there has been an increased focus on the link between the history of preeclampsia and cardio metabolic syndrome - a danger signaling event. The impact of this event is now becoming alarming in developing countries but data is scanty. Hence the need to collate information in Ghana.

Aim: To compare cardio metabolic profile of preeclampsia before and after 34 weeks in Ghana

Methodology: The nested case control study was located at the Obstetrics and Gynecology department of the Korle-Bu Teaching Hospital (KBTH). One hundred and sixty-four (164) consented subjects were recruited after ethical clearance was obtained and structured questionnaire administered to them. Four (4) ml blood and 5 mL urine samples were taken for biochemical analysis and urinalysis respectively. Randox automated chemistry analyzer was used to quantify blood chemistry. The data was captured as protected health information (PHI) and analyzed with SPSS version 18.

Results: In preeclampsia, increased cardio metabolic scores before term were associated with low birth weight while lactate dehydrogenase (LDH) increased before 34 weeks and rather decreased after 34 weeks. Systolic blood pressure (SBP), white blood cells (WBC) and aspartate transaminase (AST) increased as well in PE clients while platelet (PLT), low density lipoprotein (LDL) and birth weight decreased when these variables were doubly stratified by weeks of gestation and cardio metabolic profile.

Conclusion: Among preeclampsia, increased cardio metabolic profile before term were associated with low birth weight.

Introduction

Cardio metabolic syndrome [1-5] is a danger signaling [6] event that is generated from trauma and or tissue damage or cellular death resulting from lactate dehydrogenase (LDH) leakage [7] from the cell. This signaling event revolves round the interplay between metabolic factors and cytokines which activates the immune system [6] through inflammatory nutrients [8] or fatty meals [9,10] or excess anti-inflammatory nutrient due to dose dependent loss of specificity [8]. The metabolic factors include high blood pressure, increased insulin levels, increased body mass index (BMI), and abnormal cholesterol levels [1-5,11]. These factors independently lead to clinical array of diseases such as diabetes, stroke, cardiovascular disorders, dyslipidemia and or hypercholesterolemia [1-5,11]. The disease conditions are as a result of (i) a modification of low density lipoprotein (LDL) to oxidize - LDL (ox-LDL) [12-17] in the endothelial system leading to its impairment [18]; or (ii) induction of monocyte chemotactic protein 1 (MCP-1) by ox-LDL [19]; or (iii) recruitment of monocytes and T-cells to the intima by ox-LDL that promotes the transformation of monocytes to macrophages [16]. Ox-LDL, together with angiotensin II, TNF-α and or local stress also induce lectin-like ox-LDL receptor 1 (LOX-1) in the endothelial system causing its impairment [18]. A potent agonist of ox-LDL is peroxisome proliferator-activated receptor (PPAR-γ), a lipid sensing ligand activated transcription factor [20-27] which binds to toll-like receptors (TLR) [28,29] and initiate a cellular response leading to activation of NF-κB and regulation of immune responsive genes. PPAR-γ is therefore involved in lipid metabolism, glucose homeostasis and inflammatory activity [24] through activation of NF-κB. Under extremely abnormal circumstances, immune responsive genes finds alternate routes thereby increasing protein catabolism (e.g. excretion of long or short polypeptide chains in urine) or increasing gluconeogenesis. Both protein catabolism and increased gluconeogenesis could affect maternal and perinatal outcomes of pregnancy.

However, it remains unclear whether pregnancy induced hypertensive women and or preeclampsia have altered levels of

cardio metabolic profiles before pregnancy or whether the conditions arise due to disturbances induced by the pregnancy itself. A better understanding of the underlying pathophysiology of preeclampsia (PE) is therefore needed for early intervention. Cardiometabolic profile might provide such platform of data support, since increasing risk is seen in the pathogenesis of PE.

PE is a multifactorial disorder with no specific identifiable etiology and accounting for 5-7% of all pregnancies with significant maternal and perinatal morbidity and mortality [30-31]. Most of the studies into the etiology and the pathogenesis of preeclampsia [30-32] had been conducted in the developed world with limited data in the developing countries such as Ghana. It is therefore imperative that such studies be replicated in our indigenous women to provide evidence base information to aid in the prevention and management of preeclampsia and its complications. The current research thereby seeks to investigate the role of cardio metabolic risk on the pathogenesis and outcomes of PE in the Ghanaian population.

Aim: To compare cardio metabolic profile of preeclampsia before and after 34 weeks in Ghana

Method

Anthropometry: A questionnaire for clinical information was obtained after informed consent and ethical review (**MS-Et/M.3 – P.3.2/2013 – 2014**) for this nested case-control study situated at the Obstetrics and Gynecology unit, Korle-Bu teaching hospital, Accra. The sample consisted of 164 participants; fifty-five (55) controls, fifty-five (55) pregnant normotensives and fifty-four (54) PE.

Dependent variable: Cardio metabolic profile

Independent variables: Body mass index (BMI), Age, blood pressure, creatinine, lactate dehydrogenase, week of gestation, lipid profile and full blood count (FBC).

Term pregnancy: Gestational age of 37 weeks and above

Case definition: Metabolic syndrome was defined in accordance with NCEP - ATP III [11] as the presence of three (3) or more of the following characteristics:

i.   Waist circumference > 102 cm in men and > 88 cm in women

ii.   Triglyceride levels ≥ 150 mg/dl,

iii. High density lipoprotein cholesterol < 50 mg/dl in women

iv.   Blood pressure ≥130/85 mm Hg

v.   Fasting serum glucose ≥110 mg/dl.

Cardio metabolic scoring profile: Each risk factor of cardio-metabolic profile was divided into the categories shown in Table 1.

Inclusion and exclusion criteria: Only patients diagnosed with PE were recruited after obtaining their consent as cases. Control subjects included normotensive pregnant and non-pregnant women who gave informed consent. Patients with a history of renal disease, chronic hypertension, diabetes, molar pregnancy, urinary tract infection, thyroid dysfunction and infectious diseases were excluded.

Blood collection and processing: Four milliliter (4 ml) blood was drawn from an antecubital vein by means of a plastic syringe and dispensed into EDTA (for FBC) and gel tubes taking careful precautions. Sysmex hematological auto analyzer was used to quantify FBC whilst RANDOX auto analyzer was used for the determination of lipid profile, LDH and creatinine levels.

Urinalysis: Five mL spot urine was obtained to determine proteinuria and to categorize subjects into normotensives and PE.

For the purposes of this study, PE was defined based on American College of Obstetricians and Gynecologist criteria. Accordingly, PE is defined as diastolic blood pressure of ≥ 90 mmHg and or systolic blood pressure of ≥140 mmHg with proteinuria ≥300 mg/dl occurring after 20 weeks of gestation.

Data management

The integrity of patient records, ethics and data protection were taken into consideration. Data were created on a spreadsheet, corrected for errors, three (3) different backups created and SPSS version 18 used for analysis.

Results

The study was completed by 164 subjects (Table 2). The ratio of pregnant normotensives to controls to PE was 1:1:1 respectively. Majority of the subjects were close to the study site, Accra (Table 2) with few exceptional referral PE cases from other parts of the country. All subjects attained at least some level of education while artisan formed the major occupation of these subjects. Significant statistical differences were observed in a major number of clinical variables studied except BMI (Table 3). Also, with the exception of a decreased platelet among PE clients; systolic blood pressure (SBP), diastolic blood pressure (DBP), liver enzymes, urine protein, urine pH, white blood cells (WBC), lipids, lactate dehydrogenase (LDH) and cardio metabolic profile significantly increased. However, when some of these variables were doubly stratified by the weeks of gestation and cardio metabolic profile; SBP, WBC and aspartate transaminase (AST) increased in PE clients while platelet (PLT), low density lipoprotein (LDL) and birth weight decreased (Table 4). LDH, on the other hand, increased with lesser weeks of gestation and rather decreased after 34 weeks in PE subjects. The hypothesis that cardio metabolic profile contributes significantly to the pathogenesis and outcomes of PE was also tested (Table 4 and 5). Table 1 scoring system was used in calculating cardio-metabolic profile.

Discussion

In this study, a report on the association of cardio metabolic

Table 1. Cardio metabolic profile scoring system.

Age (years)	score	Smoker	score	LDL (mg/dL)	score	HDL (mg/dL)	score	TG (mg/dL)	score	SBP (mmHg)	score
18-22	0	No	0	<100	0	<35	11	<100	0	<120	0
23-27	6	Yes	8	100-129	5	35-44	8	100-149	2	120-129	2
28-32	11			130-159	10	45-54	5	150-199	3	130-139	3
33-37	16	**Drinking**	score	160-189	14	≥55	0	≥200	4	140-159	5
38-42	21	No	0	≥190	20					≥160	8
43-47	26	Yes	8								

1 mmol/L=18 mg/dL**;** SBP=systolic blood pressure; DBP=diastolic blood pressure; HDL=high density lipoprotein; LDL=low density lipoprotein; TG=triglyceride

Table 2. Study demographics.

	Preg. Normotensive [55]	Control [55]	Preeclampsia [54]
Residing in			
Greater Accra	49(89.0)*	50(90.9)	25(46.3)
Central	6(10.9)	5(9.1)	5(9.3)
Other			24(44.4)
Tribe			
Akan	25(45.5)	5(9.1)	15(27.8)
Ga	13(23.6)	32(58.2)	6(11.1)
Ewe	8(14.5)	5(9.1)	7(13.0)
Frafra	4(7.3)	6(10.9)	5(9.3)
Fante	5(9.1)	3(5.5)	1(1.9)
No answer		4(7.3)	20 (37.0)
Education			
Primary	6(10.9)	6(10.9)	9(16.7)
Junior	14(25.5)	21(38.2)	10(18.5)
Senior	14(25.5)	16(29.1)	9(16.7)
Tertiary	21(38.2)	13(23.6)	4(7.4)
No answer			22(40.7)
Occupation			
Artisan	34(61.8)	34(61.8)	25(46.3)
Nurse	6(10.9)		2(3.7)
Housewife	4(7.3)		
Banker	2(3.6)		
Student	2(3.6)	8(14.5)	
Teacher	7(12.7)	4(7.3)	1(1.85)
No answer		9(16.4)	24(44.4)
Unemployed			2(3.7)

* Number (%)

Table 3. Clinical variable in the study.

	Pregnant normotensive	Control	Preeclampsia	ANOVA p-value	Preg. Normo x control (p-value)	PE x control (p-value)	PE x preg. Normo (p-value)
Age (years)	27.87 ± 4.21(**55**)¥	34.50 ± 8.79(**55**)	30.95 ± 6.00(40)	0.000	0.000	0.030	0.004
BMI (kg/m²)	29.40 ± 6.40(**55**)	27.60 ± 6.32(**55**)	28.90 ± 6.30(32)	0.318	0.141	0.357	0.725
SBP (mmHg)	108.65 ± 17.65(**55**)	108.67 ± 21.20(48)	139.80 ± 33.80(42)	0.000	0.996	0.000	0.000
DBP (mmHg)	69.76 ± 12.67(**55**)	70.50 ± 12.63(48)	90.20 ± 26.00(42)	0.000	0.768	0.000	0.000
Alanine aminotransferase (U/L)	6.11 ± 3.40(53)	15.87 ± 5.36(**55**)	12.37 ± 17.32(47)	0.000	0.000	0.158	0.011
Aspartate aminotransferase (U/L)	13.02 ± 3.87(53)	24.67 ± 9.07(**55**)	39.18 ± 33.71(47)	0.000	0.000	0.003	0.000
Urine protein	10.64 ± 7.04(**55**)	7.07 ± 5.58(53)	163.90 ± 124.90(33)	0.000	0.004	0.000	0.000
Urine pH	5.80 ± 0.85(**55**)	5.40 ± 0.79(53)	6.04 ± 0.824(33)	0.002	0.013	0.001	0.198
Specific gravity	1.01 ± 0.01(**55**)	1.02 ± 0.01(53)	1.02 ± 0.05(33)	0.323	0.000	0.773	0.464
WBC (x10⁹/L)	7.80 ± 1.63(**55**)	5.73 ± 1.42(53)	9.40 ± 3.90(43)	0.000	0.000	0.000	0.007
RBC (x10¹²/L)	4.00 ± 0.47(**55**)	4.64 ± 0.39(53)	4.70 ± 1.50(43)	0.000	0.000	0.780	0.002
PLT (x10⁹/L)	242.00 ± 70.80(**55**)	297.45 ± 82.10(53)	221.40 ± 93.20(43)	0.000	0.000	0.000	0.217
Hb (g/dL)	11.00 ± 2.39(**55**)	12.98 ± 1.3853)	12.40 ± 3.10(43)	0.000	0.000	0.225	0.013
Creatinine (µmol/L)	52.60 ± 17.30(40)	68.80 ± 10.95(53)	64.20 ± 20.80(49)	0.000	0.000	0.161	0.006
Cholesterol (mmol/L)	5.23 ± 1.20(40)	4.50 ± 1.22(53)	5.52 ± 1.40(**54**)	0.000	0.005	0.000	0.295
Triglycerides (mmol/L)	1.88 ± 0.63(40)	0.72 ± 0.43(53)	2.00 ± 0.96(**54**)	0.000	0.000	0.000	0.493
HDL (mmol/L)	1.25 ± 0.37(40)	0.95 ± 0.40(53)	1.51 ± 0.42(**54**)	0.000	0.000	0.000	0.002
LDL (mmol/L)	4.10 ± 1.17(40)	3.08 ± 1.20(53)	3.70 ± 1.50(**54**)	0.001	0.000	0.020	0.165
LDH (U/L)	232.10 ± 68.30(40)	346.20 ± 145.40(50)	307.90 ± 160.50(49)	0.000	0.000	0.216	0.007
Cardiometabolic profile	19.70 ± 3.50(40)	17.30 ± 9.40(53)	21.00 ± 8.50(54)	0.051	0.128	0.035	0.365

¥ Mean ± standard deviation (number); BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; WBC=white blood cell; RBC=red blood cell; PLT= platelet; Hb= hemoglobin; HDL=high density lipoprotein; LDL=low density lipoprotein; LDH=lactate dehydrogenase

profile '***before and after***' 34 weeks and adverse pregnancy outcomes were presented. We found significantly increased cardio metabolic profile before term was associated with low birth weight. We have also formulated a sensitive but simple method of calculating cardio metabolic profile to aid clinicians in assessment of future risk of developing the syndrome in PE. This study adds unto the existing knowledge elsewhere that the relationship between cardio metabolic scores and adverse pregnancy outcomes were inversely related [33,34].

Barden and others [35] also suggested that predisposition to metabolic syndrome sensitized women to develop preeclampsia. Even though the present study depicted this trend, lack of extensive patient follow-ups and their relocation and or moving back to their various destinations affected further sampling parameters. Notwithstanding, data from Norwegian research indicated a two-fold and four-fold increase of PE with body mass index (BMI >27.08 kg/m²) and blood pressure (SBP >121 mmHg and DBP > 71 mmHg) respectively [36]. A meta-analysis had also confirmed the relationship of hypertension to lower birth weight and head circumference, as well as the importance

Table 4. Cardio metabolic profile, weeks of gestation and some indicators.

s	20 ≤ x < 34 weeks						x ≥ 34 weeks					
	<20 cardiomet score		*P-value*	>20 cardiomet score		*P-value*	<20 cardiomet score		*P-value*	>20 cardiomet score		*P-value*
	Preg. normo	PE		Preg. normo	PE		Preg. normo	PE		Preg. normo	PE	
Gravidity	2.48 ± 1.47 (23)	2.00 ± 1.41 (7)	0.452	2.31 ± 1.54 (13)	3.4 ± 0.89 (12)	**0.043**	2.52 ± 1.63 (21)	3.33 ± 1.15 (4)	0.356	1.89 ± 1.27 (9)	2.50 ± 2.12 (11)	0.459
Parity	2.26 ± 1.39 (23)	1.00 ± 1.41 (7)	**0.046**	0.93 ± 1.43 (14)	1.40 ± 1.34 (12)	0.398	1.33 ± 1.53 (21)	2.00 ± 1.73 (4)	0.439	0.67 ± 0.71 (9)	1.50 ± 2.12 (11)	0.278
Birth weight (g)	2578.33 ± 861.31 (9)	1900.00 ± 1272.00 (7)	0.224	2575.00 ± 499.15 (4)	750.00 ± 353.55 (2)	**0.010**	2566.67 ± 1267.54 (6)	2733.30 ± 808.3 (3)	0.844	3000.00 ± 346.41 (3)	-	-
SBP (mmHg)	109.65 ± 16.81 (19)	135.60 ± 34.45 (7)	**0.016**	95.43 ± 28.67 (14)	154.5 ± 22.29 (10)	**0.000**	113.65 ± 15.91 (17)	143.0 ± 37.64 (4)	**0.021**	166.19 ± 27.69 (9)	163.3 ± 23.98 (9)	0.815
LDH (U/L)	230.50 ± 89.08 (6)	381.63 ± 185.16 (7)	0.096	235.08 ± 65.34 (14)	370.14 ± 158.62 (12)	**0.007**	201.60 ± 65.22 (5)	207.97 ± 5.46 (4)	0.853	477.91 ± 709.95 (9)	220.96 ± 93.34 (10)	0.271
LDL (mmol/L)	3.78 ± 0.78 (6)	2.88 ± 0.89 (7)	0.081	4.58 ± 1.00 (14)	3.17 ± 1.16 (12)	**0.002**	3.91 ± 0.89 (5)	4.20 ± 0.78 (4)	0.625	3.94 ± 1.49 (9)	2.92 ± 1.17 (10)	0.113
WBC (x10⁹)	8.27 ± 1.56 (22)	8.34 ± 3.55 (7)	0.941	8.15 ± 2.91 (13)	10.81 ± 4.82 (10)	0.115	7.72 ± 1.19 (21)	7.79 ± 2.80 (4)	0.933	7.37 ± 2.18 (9)	8.23 ± 4.12 (9)	0.587
PLT (x10⁹)	248.72 ± 78.92 (22)	188.83 ± 49.10 (7)	0.071	248.85 ± 59.24 (13)	279.10 ± 86.47 (10)	0.330	239.38 ± 72.26 (21)	192.00 ± 104.06 (4)	0.272	262.44 ± 84.25 (9)	202.89 ± 82.78 (9)	0.149
AST (U/L)	12.15 ± 2.84 (17)	38.38 ± 31.61 (7)	**0.002**	13.14 ± 4.31 (7)	56.44 ± 53.61 (12)	0.050	13.72 ± 4.64 (11)	26.93 ± 18.08 (4)	**0.000**	15.53 ± 6.09 (8)	44.79 ± 28.81 (10)	**0.012**

cardiomet = cardio metabolic; AST=aspartate dehydrogenase

Table 5. Cardio metabolic profile and birth weights from PE subjects.

	Birth weight (g)	
<20 cardiomet score	2220.00 ± 978.43 (10)	$t_{10, 724.2}$ = 2.03
>20 cardiomet score	750.00 ± 353.55 (2)	
p-value	0.0698	

of catch-up growth [37]. However, when this same type of analysis were restricted to studies with published correlations between systolic BP and birth weight, the association was not so strong; an indication of other eminent factors [1-5,11] in the environ which could possibly cause such effects [37,38].

There is also evidence outside of pregnancy that increased leukocyte counts within normal range were associated with metabolic disorders in women [39,40]. Other findings suggested that slightly increased leukocyte counts may modestly be associated with the development of pregnancy induced hypertensive disorder. However, leukocyte count alone was relatively a non-specific marker of inflammation due to it being influenced by other factors such as infection and certain medications [41]. Data from Kaiser Permanente MHC also showed that inflammation as measured by increased leukocytes was predictive of hypertension but were unable to present the potential mechanism [42,43]. We are by this study suggesting that preeclampsia (PE), through the cardio metabolic signaling pathway was as a result of the modification of LDL to form ox-LDL which did trigger foam cell formation. This was because of the relatively low LDL levels observed. Current literature also suggested that upon activation of macrophage system (foam cells) by ox-LDL [12-19], primary mediators like cytokines or chemokines elicited the recruitment of secondary mediators e.g. white blood cells (WBC) to thus impair the endothelial system.

Despite the well-intentioned efforts at making laboratory diagnosis of PE and it complications especially HELLP syndrome (Haemolysis, Elevated liver enzymes and low platelets) based on the presence of hemolysis, elevations of liver enzymes (AST, ALT), LDH and proteinuria, substantial inter-laboratory differences remain a major problem. This was partly due to the cutoff point or reference ranges used to establish an abnormal test and the different number of assays used to measure these tests. In this study, the standardized hospital protocol was used to ascertain the various parameters.

Conclusion

In preeclampsia, increased cardio metabolic profiles before term were associated with low birth weight.

Acknowledgement

Funding disclosure

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