Plasma C-Reactive Protein and Selected Nutritional Indices in Elective Caesarean Section

Kayode S Adedapo[1], L N Nwobi[1], Oladapo Olayemi[2], Christopher O Aimakhu[2], Olayinka O Ogunbode[2], A F Akinboade[2], Francis A A Adeniyi[1]
Departments of [1]Chemical Pathology and [2]Obstetrics and Gynaecology, College of Medicine, University of Ibadan, University College Hospital, Ibadan, Nigeria

Abstract
Context: Caesarean Section (CS) is a major surgical procedure, often performed when a vaginal delivery is considered unsafe.
Objective: This study was carried out to understand the interaction between acute phase proteins and nutritional factors consequent to caesarean section. The knowledge of this interaction is important for successful management of these patients.
Methods: Plasma samples from fifty (50) pregnant women booked for elective caesarean section in Ibadan, Nigeria were collected on the day preceding surgery, one day and four days post-surgery to determine the levels of CRP, vitamin C, PCV, Total protein, albumin and globulin (Glb) levels.
Results: The mean age of the patients studied was 32.29 ± 3.66 years, range; 24 39 years. Significant elevations were observed in the levels of TP, Glb and CRP one day post-surgery (1DPS) compared with baseline (BS) (7.36 ± 1.46) vs 6.56±1.30, (4.68 ± 1.33) vs 2.70±1.51, (111.43 ± 68.89) vs 6.00 ± 13.27 respectively, while albumin reduced significantly (2.68 ± 1.08) vs 3.87±0 .63. Similar changes were observed on day 4. There was no significant change in the levels of Vitamin C.
Conclusion: One of the positive predictive indicators of good outcome after caesarean delivery is adequate nutrition.
Key Words: Elective caesarian section, acute phase proteins, nutritional factors

Introduction
A caesarean section (CS) is a major surgical procedure often performed when a vaginal delivery would put the baby's or mother's life or health at risk. It may be performed at short notice, particularly if there are complications or difficulty in labour (emergency section) or planned in advance (elective section). An elective caesarean section is performed one to two weeks before the baby's due date and this ensures the baby is mature before delivery. Reasons for elective caesareans vary, with a key distinction being between hospital or doctor-centric reasons and mother-centric reasons.[1,2]

One of the greatest expectations after surgery is effective and rapid wound healing whose ultimate outcome is repair of tissue defect[3], this results in increased cellular activity, with an intensified metabolic demand for nutrients [4], thereby influencing the outcome of the damaged tissue. Adequate nutrition promotes wound healing as it provides the raw materials needed for wound repair, enhances immunocompetence, decreases susceptibility to infection, and optimizes the patient's healing outcome[5]

Oxygen supply is vital to healing hence; anaemia which results when there is inadequate haemoglobin to carry oxygen to body tissues is inimical to wound healing[6]. Anaemia goes undetected in many people, and symptoms can be minimal and vague. Anaemia is a relative contraindication for elective surgery. [7] Packed cell volume (PCV) is one of the indices used in diagnosing anaemia.

The acute phase plasma protein response is part of the complex series of physiological, hematological, and biochemical events that constitute the inflammatory response after

Correspondence: Dr K S Adedapo,
Department of Chemical Pathology,
University College Hospital, PMB 5116
Ibadan, Nigeria.
E-mail: ksadedapo@yahoo.com;
kadedapo@comui.edu.ng

tissue injury or infection. The magnitude and duration of the response are related to the nature and severity of the injury. There is also increase in acute-phase protein production in response to stress such as surgery, and amino acid mobilization from muscle used for hepatic gluconeogenesis[4]. CRP is widely regarded as a positive reactant and one of the most sensitive and specific markers of the acute phase protein response (APPR), since its plasma concentration in health is very low, whereas infection or trauma may stimulate an increase of several hundred fold. [6] Malnutrition is also known to affects the level of plasma C-reactive protein[8].

For successful management of surgical patients therefore, it is important to understand the interaction that exists between acute phase proteins and nutritional factors consequent to caesarean section.[4] While the effect of nutritional status on wound healing is well documented, its changes before and after caesarean section requires further assessment in order to predict a defective healing outcome. This therefore, served as the basis of this research work.

Materials and Methods

The levels of C-reactive protein (CRP), total protein (TP), albumin (Alb), globulin (Glb), vitamin C and packed cell volume (PCV) were determined in fifty (50) pregnant women who were booked for elective caesarean section from the department of Obstetrics and Gynaecology, University College Hospital, Ibadan, Nigeria. An ethical approval was obtained from the joint UI/UCH Research Ethics Committee. Informed consent was obtained from each patient before sample collection and the need for the study was explained in local language when necessary. All pregnant women booked for elective caesarean section with, multiple pregnancy, HIV-infection or other severe viral infections, any form of malignant disease, recent exposure to chemotherapy or radiotherapy, gestational diabetes, previous history of diabetes, hypertension and special medication were excluded from the study.

Ten milliliters (10 ml) of venous blood samples were obtained from each subject using standard venepuncture technique before surgery, one day, and four days post-surgery into heparinized bottles. Each patient served as her own control. All blood samples were centrifuged (1163 Õ g for 5 minutes), aliquoted into 3 plain bottles (sample for Vit. C was stabilized and protected from oxidation) and stored at -20°C until analysis. Blood from a lancet finger prick from each patient collected in Na-heparinized capillary tubes was used for immediate PCV determination.

The parameters were analyzed using semi-quantitative method for CRP, HPLC for vitamin C, standard haematological procedures for PCV, standard spectrophotometric methods for essential trace elements, total protein and albumin. The difference between the levels of TP and Alb was used to calculate the globulin levels. Surgical wounds from surgery were assessed visually by a Senior Registrar on the 4th day before discharge.

Data was analyzed using SPSS version 15.0. Student's t-test (paired) was used for the comparison of quantitative variables.

Results

The mean age of the subjects was 32.29 ± 3.66 years, range; 24-39 years. All of these women were middle level income earners and all of them had post secondary school education.

Significant elevations were observed in the mean levels of TP 7.36 ± 1.46 vs 6.56±1.30, Glb 4.68 ± 1.33 vs. 2.70±1.51, and CRP 111.43 ± 68.89 vs. 6.00±13.27 one day post-surgery (1DPS) compared with baseline (BS), while the mean albumin level reduced significantly 2.68 ± 1.08 vs. 3.87±0 .63. [Table 1].There was no significant change in the levels of Vitamin C. Comparing the baseline with the samples collected on 4th day post operation, the levels of TP 7.47 ± 1.10, Glb. 4.45 ± 1.16 and CRP 139.64± 162.28 increased significantly [Table 2]. The level of albumin however decreased significantly 2.94 ± 0.53 vs. 3.87±0 .63. Again, there was no significant change in Vitamin C level. Similar trend of changes was observed when the 4DPS samples were compared with 1DPS. No significant difference was observed between the mean levels of PCV at baseline and one and four day post-surgery implying negligible blood loss. All the wounds healed well while estimated blood loss was minimal in all cases.

Table 1. Comparison of the mean levels of total protein (TP), albumin (Alb) and globulin (Glb) before (BS), one and four days post-surgery (4DPS).

Period	TP(g/dL)	t	p	Alb(g/dL)	t	p	Glb(g/dL)	t	p
BS	6.56±1.30			3.87±0.63			2.70±1.51		
Vs		2.116	*0.044		5.697	*0.000		5.474	*0.000
1DPS	7.36±1.46			2.68±1.08			4.68±1.33		
BS	6.56±1.30			3.87±0.63			2.70±1.51		
Vs		2.915	*0.007		5.635	*0.000		4.453	*0.000
4DPS	7.47±1.10			2.94±0.53			4.45±1.16		
1DS	7.36±1.46			2.68±1.08			4.68±1.33		
Vs		0.272	0.787		1.065	0.296		0.596	0.556
4DPS	7.47±1.10			2.94±0.53			4.45±1.16		

*p is significant á<0.05 value (2-tailed)

Table 2. Comparisons of the mean levels of vitamin C and CRP before surgery, one and four days post-surgery.

Period	Vit C(mg/L)	t	p	CRP(mg/L)	t	p
BS	0.48±0.15			6.00±13.27		
Vs		1.552	0.132		7.737	*0.000
1DPS	0.54±0.17			111.43±68.89		
BS	0.48±0.15			6.00±13.27		
Vs		1.912	0.067		4.298	*0.000
4DPS	0.55±0.15			139.64±162.28		
1DS	0.54±0.17			111.43±68.89		
Vs		0.231	0.819		0.899	0.377
4DPS	0.55±0.15			139.64±62.28		

*p is significant á<0.05 value (2-tailed)

Discussion

Pregnancy is associated with a series of small, continuous physiologic adjustments that affect the metabolism of all nutrients. These processes account for the raised metabolic rate (hypermetabolic state) in the pregnant state. [9] This metabolic modulation during pregnancy is further exacerbated post-surgery and characterized by release of adrenal and pituitary mediators, leading to an increase in protein and lipid catabolism. Other changes are non-glucose related hyperglycaemia and salt and fluid retention[10]

Following surgery, various immunological, inflammatory and metabolic changes occur to promote repair and healing. Recovery from

surgery depends on the body nutritional status before, during, and after surgery. Malnutrition, either before or after surgery, has a negative effect on recovery from surgery.[11] Nakamura[12] reported that being malnourished prior to surgery was associated with increased post-operative inflammation. It was also observed that surgical patients who were better nourished prior to surgery had shorter hospital stay and required less intensive post-surgery care .[13]

In this study, significant increase in the level of total protein was found in day one and day four post surgery compared to baseline. The observed increase may be due to increased synthesis of positive acute phase proteins such as C-reactive proteins, serum amyloid A and complement factors. This increase may override the simultaneous decrease in negative acute phase proteins such as albumin. This increase could also be as a result of increase in globulins. Globulin level showed a significant increase in day one and day four when compared with the baseline. The observed pattern of increase is a direct reflection of increased synthesis of acute phase proteins such as CRP, coagulation and complement proteins that come to play during acute inflammatory processes all of which are found in the globulin portion of protein.

These observations contradict the findings of Nielsen[14] who reported a decrease in total protein level one day post post-surgery but a return towards the pre-operative level four days post-surgery in patients undergoing abdominal aorta reconstructive surgery which may involve much blood loss compared to elective caesarian section in well trained hands.

Albumin level showed a significant decrease in day one and day four as compared with the baseline. The observed pattern of decrease could be attributable to dilution effect secondary to intravenous infusion of saline and glucose solutions during surgery and in the immediate post-operative period. Although water excess is rapidly eliminated, sodium overload is slowly excreted, leading to more prolonged extracellular fluid dilution and, as a consequence, albumin dilution. It could also be due to tissue and systematic inflammatory reactions that occur during major trauma, like surgery, which causes redistribution of albumin from the plasma to the wound site.[15] The reduction may also be due to increased synthesis of local inflammatory mediators (acting on the capillary wall) which leads to increased transcapillary escape of proteins such as albumin.[16] The severity of the injury is proportional to increase in vascular permeability or alterations in intestinal permeability which has been associated with major surgery.[17] More so, it could be due to increased albumin catabolism. These observations agree with several reports[18-21] The fairly stable state of Vitamin C pre and post surgery in all patients may be because many pregnant women are likely to be on micronutrients supplement during pregnancy. It could also be a reflection of adequate dietary intake during pregnancy.

.

C-reactive protein showed a significant increase in day one and fourth day post surgery compared to the baseline. The progressive rise was consequent to increased hepatic synthesis of inflammation-associated cytokines such as IL-6 after surgery. The increase in CRP level is required for opsonization of dead cells, in turn amplifying and focusing inflammatory response on dead and damaged tissue. The observed result was in accordance with reports elsewhere[22, 23,24].

The lack of statistically significant change in the levels of PCV before surgery, one and four day post-surgery observed probably indicates that the patients were not anaemic before or after the surgery and invariably satisfactory nutritional status in all of them. Furthermore it is an indication of minimal blood loss in all the patients studied. In this study all the patients that completed the study were discharged home fourth day post surgery without wound infection or dehiscence due to fairly good nutritional status.

In conclusion, the observed variations in the levels of the studied parameters may be useful as early indices for normal wound healing since all the studied subjects had satisfactory wound healing. Given the good nutritional status of these patients all of whom were middle level income earners and all of who have had post secondary school education, thus all are well informed and comfortable enough to afford elective surgery, it could be said that one of the positive predictive indicators of good surgery apart from the surgeon is adequate nutrition.

Trop J Obstet Gynaecol, 26 (1), April 2009. ISSN 0189 5178

References

1. Savage W. The rising caesarean section rate: a loss of obstetric skill? *J Obstet Gynaecol.* 2007; 27(4): 339346.
2. Lee Y.M., D'Alton M.E. Cesarean delivery on maternal request: maternal and neonatal complications. *Curr Opin Obstet Gynecol.* 2008; 20(6): 597-601.
3. Stadelmann W.K., Digenis A.G., Tobin G.R. Physiology and healing dynamics of chronic cutaneous wounds. *The American Journal of Surgery* 1998; 176 (2): 26S-38S.
4. Mackay D. and Miller A. Nutritional support for wound healing. *Alternative Medicine Review* 2003; 8(4): 359-377.
5. William E.B., Michael Y.H., Ashima M., Pramela R. Serial Serum C-Reactive Protein levels in the diagnosis of neonatal infection. *Pediatrics*. 2000; 102(4): 41.
6. Thompson D., Milford-Ward A., Whicher J.T. The value of acute phase protein measurements in clinical practice. *Ann Clin Biochem*. 1992; 29: 123-131.
7. World Health Organization 2008. Worldwide prevalence of anaemia 1993-2005.
8. Curtis G.E., Mc Atear C., Formela L., Walsh A., Shenkin A. The effect of nutritional status on the cytokine and acute phase protein: Responses to Elective Surgery. *Cytokine*. 1985; 7(4): 380-388.
9. Anetor J.I., Adelaja O., Adekunle A.O. Serum micronutrient levels, nucleic acid metabolism and antioxidant defences in pregnant Nigerians: Implications for fetal and maternal health. *Afr. J. Med. Med. Sci.* 2003; 32: 257-262.
10. Putwatana P., Revdecha P., Sirap-ngam Y., Lertsithichai P., Sumbonnanonda K.. Nutritional Screening tools and the prediction of postoperative infections and wound complications: Comparison of methods in presence of risk adjustment. *Nutrition* 2005; 21(6): 691-697.
11. Reiland K.E. Gastrointestinal Surgical patients' outcomes influenced by nutrition. *AORN J*. 2000; 71: 199-204.
12. Nakamura K., Moriyama Y., Kariyazono H. Influence of preoperative nutritional state on inflammatory response after surgery. *Nutrition*. 1999; 15: 834-841.
13. Mazolewski P., Turner J.F., Baker M. The impact of nutritional status on the outcome of lung volume reduction surgery: a prospective study. *Chest*. 1999; 116: 693-696.
14. Nielsen O.M. Sequential changes in circulating total protein and albumin masses after abdominal vascular surgery. *Ann. Surg.* 1985; 231-234.
15. Smith P.C., Frank H.A., Kasdon E.J.. Albumin uptake by skin, skeletal muscle and lung in living and dying patients. *Ann Surg*. 1978; 187: 31-37.
16. Fleck A., Colley C.M., Myers M.A.. Liver export proteins and trauma. *Brit Med Bull* 1985; 41: 265-273.
17. Tannus A.F., Valenca de Carvalho R.L., Suen V.M., Cardoso J.B., Okano N., Marchini J.S. Energy expenditure after 2- to 3-hour elective surgical operations. *Rev Hosp Clin Fac Med Sao Paulo*2008; 56(2): 37-40.
18. Rehm M., Haller M., Orth V., Kreimeier U. Jacob M., Dressel H., et al. Changes in blood volume and hematocrit during acute preoperative volume loading with 5% albumin or 6% hetastarch solutions in patients before radical hysterectomy. *Anesthesiology*. 2001; 95(4): 849-856.
19. Rodoman G.V., Dobretsov G.E., Shalaeva T.I., Naumov E.K. Albumin fluorescent test in surgical stress. *Bull Exp Biol Med* 2001; 131 (3): 302-304.
20. Barle H., Hallstrom L., Essen P., Thorne A., McNurlan M.A., Garlick P.J. The synthesis rate of albumin decreases during laparoscopic surgery. *Clin Physiol Funct Imagin* 2004; *24*(2): 91-95
21. Alberti L.R., Petroianu A., Velsoso D.F. The effect of surgical trauma in post-operative albumin concentration after major surgeries. *Einstein* 2009; 71(1): 48-51.
22. Cruickshank A.M., Fraser W.D., Burns H.J., Van D.J., Shenkin A. Response of serum interleukin 6 in patients undergoing elective surgery of varying severity. *Clin Sci*. 2009; 79: 161-165.
23. Ohatzo H., Yoshizaki K., Nishimoto N. Interleukin-6 as a new indicator of inflammatory status: detection of serum levels of interleukin-6 and C-reactive protein after surgery. *Surgery* 1992; 111 (2): 201-209.
    Choileain N.N., Redmond H.P. Cell response to surgery. *Archives of surgery.* 2006; 141(11): 1132-1140.