ORIGINAL ARTICLE

ASSOCIATION OF LIVER FATTY ACID BINDING PROTEIN WITH ACUTE KIDNEY INJURY IN PAEDIATRIC PATIENTS AFTER CARDIAC SURGERY

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Background: Acute kidney injury (AKI) is a common complication after cardiac surgery. Like Creatinine level, the role of L-FABP in renal injury and its recovery had been shown by studies, so by using/measuring urinary Liver fatty acid-binding protein (uL-FABP) levels it can be a valuable biomarker for monitoring and diagnosis of various renal diseases. The study aimed to determine L-FABP as a biomarker for early diagnosis of AKI acute kidney injury in paediatric patients after cardiac surgery so that early treatment interventions can prevent AKI morbidity. **Methods**: This descriptive study was conducted in the Pathology laboratory of Sheikh Zayed Hospital, Lahore from 2015 to 2016. Selected through convenience sampling, patients' blood and urine were analysed for desired markers. **Results:** Out of 88, 10 (11.4%) patients developed AKI after cardiac surgery. In patients with AKI, serum creatinine levels started to rise at 24–48 h after surgery whereas uL-FABP was to be high at 4h. The optimal cut-off value of uLFABP was found 269 ng/l, with this cut-off value sensitivity of marker at four hours to recognize AKI was found to be 80% and specificity was 83.3%, the positive and negative predictive values were 38.1% and 97.0% respectively with an accuracy level 83.0%. **Conclusion:** It may be concluded from this study that uL-FABP may be considered as an early predictor of the development of AKI in paediatric patients undergoing cardiac surgery.

Keywords: Acute kidney injury; Urinary Liver Fatty Acid Binding Protein; Cardiac surgery; Biomarker; Sensitivity; Specificity

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INTRODUCTION

The kidneys are an essential organ; their main function is to remove the waste products from the blood, the regulation of electrolytes, fluids, and blood pressure, to maintain the acid-base balance, and production of various hormones. The functional unit of the kidney, the nephron is composed of a filtering unit called the glomerulus and its associated renal tubules. Through process of ultrafiltration, reabsorption and secretion, blood is cleansed, and urine is formed.[1]

Ischemia is caused by various pathophysiological conditions that can be localized or generalized. The endothelial and smooth muscle cells of blood circulation play critical part in the mechanism of AKI. Acute kidney injury (AKI) is defined as an abrupt or absolute increase in the plasma creatinine concentration of ≥0.3 mg/dL (26 μmol/L) from the baseline within 48 hours (h) or increase in plasma creatinine to ≥1.5 times from baseline, or oliguria of fewer than 0.5 ml/kg/ hour for more than 6 hours.[2] In kidney allograft transplant the decrease in the kidney blood flow detected is about 40–50%t in poorly functioning kidney[3], in many cases animals and in humans a decrease in total RBF alone cannot entirely account for the reduction in glomerular filtration rate during an episode of AKI[4,5]. In AKI the change in regional blood flow seems to have significant importance.[6] The blood flow is inapproachably decreased to the outer medulla during AKI in experimental model of animals[7,8] and probably in humans too resulting in ischemic injury to the kidney. Moreover, ischemic AKI due to endothelial cells pathology occurs in many ways[9,10].

The improper sodium uptake by proximal damaged tubules due to extra solute transport to distal nephron which is sensed by macula densa is a result of pre glomerular vasoconstriction as feedback of tubuloglomerular apparatus.[11] The local oedema which is the result of regional compromise of the blood fellow to the outer medulla secondary to arteriolar constriction resulting in pars recta intrusion within proximal tubules and the thick ascending limb, which are already normally hypoxic due to the counter current exchange properties of the vasa

recta.[12] The chances of capillary obstruction are increased in outer medulla due to their anatomical structure.[12] As a result of diminished nutrient and oxygen delivery to the epithelial cells of pars recta resulting in their inability to change from aerobic to anaerobic metabolism.[13,14]

Acute kidney injury after cardiac surgery is one of the common complications seen which is associated with adverse outcomes, including prolonged intensive care and hospital stay, diminished quality of life and increased mortality.[15] AKI occurs commonly after adult and paediatric cardiac surgeries involving about 30–40% patients.[16,17] A significant increase in mortality has been noted even after mild degrees of post-operative AKI[18] and morbidity[19]. Chronic kidney disease may develop due to episodes of AKI.[20] AKI diagnosis relies on a rise in serum creatinine concentration, which is a delayed and unreliable during acute setting.[21] The failure of interventional trials to attenuate AKI after cardiac surgery has been attributed in part to delays in diagnosis. Recent studies have focused on the discovery and validation of early biomarkers of AKI such as Liver fatty acid-binding protein (L-FABP), NGAL, IL18 and KIM1.

The L-FABP, which in humans is chiefly found in the proximal tubules mainly the straight portion and in the convoluted tubules.[22] FABP is a 14-kDa protein in mammalian intracellularly which is encoded by an enormous polygene family and is a fellow of fat binding proteins (LBP).[23] With tissue-specific expression, FABP comprises of three introns and four exons in the genes. So far nine FABPs types were discovered according to tissue-specific distribution: A (adipocyte), B (brain), E(epidermal) H (muscle and heart), IL (ileal), I (intestinal), L (liver), T (testis) and M (myelin). Intracellular transport and fatty acid metabolism are significantly regulated by all types of FABP.[24] The L-FABP consists of 127 amino acids which are found on chromosome 2 gene, including one cysteine (CYS) and three methionines (Met).[25,26] The main cause of AKI is ischemia-reperfusion (I/R) injury. Increased oxidative stress-induced due to decreased blood flow to the kidney.[27] In a pathological condition, reactive oxygen species (ROS) formed in great extent that is a far from the removing capacity of the cells.[28] Mediation of lipid peroxidation, a process in which cytoplasmic and plasma membrane, particularly lipids membrane is peroxidised via ROS.[29] Proximal tubules are damaged due to accumulation of products of peroxidation 4hydroxynonenal(4HNE) and malondialdehyde (MDA). These products along with unsaturated fatty acid are bound in the beta-sheets of L-FABP by transporting them to tubular lumen and protect the kidney from I/R injury hence interrupting the damage.[23]

Interestingly, the role of L-FABP in renal injury and its recovery had been shown by studies, so by using/measuring urinary L –FABP levels it can be a valuable biomarker for monitoring and diagnosis of various renal diseases.[30,31] This study aimed to determine if L-FABP can be used as a biomarker for early diagnosis of AKI in paediatric patients after cardiac surgery so that early treatment interventions can prevent AKI morbidity.

MATERIAL AND METHODS

This descriptive study was conducted in Pathology laboratory of Sheikh Zayed Hospital, Lahore in the department of Biochemistry and Chemical pathology with one-year duration (2015-16). Based on Non-probability convenient sampling, patients were selected from the Department of Cardio-Thoracic ward, Children Hospital Lahore. Eighty-eight patients of either gender and under 12 years of age having congenital cardiac anomalies undergoing for open-heart surgery were included in this study. Those with pre-existing renal diseases, patients on nephrotoxic drugs and fatty liver disease due to any congenital disorder were excluded. After the clearance of ethical review board patients were selected for the study from Children Hospital, Lahore, who fulfil the inclusion and exclusion criteria. Written consent was taken from the parents/guardian if they would agree to participate in this study after explaining the objectives. Their information regarding personal identity, socioeconomic background, present and past medical history along with the general physical examination was recorded and marked on the questionnaire provided. The results of the tests performed were collected and noted on the designed proforma. Patients were further divided into two groups, i.e., Patients with AKI and without AKI based on serum creatinine $\geq$0.3 mg/dl (26 µmol/l) from the baseline within 48 hours after cardiac surgery.

After aseptic measures, 1ml venous blood was collected pre-operatively and at 0, 4, 24 and 48 hours taken in a disposable syringe and collected in gel tube. 1 ml urine sample was collected in sterile container at 4 hours after cardiac surgery. Urine was centrifuged at the speed of 2000–3000 rpm for 20-minutes and venous blood at 4000 rpm for 3 minutes. The urinary samples were obtained in the Eppendorf tubes and stored at -40 °C until assays were performed. Serum samples analysis are done within 6 hours of collection. Serum creatinine was measured by Jaffe's colourimetric two-point kinetic reaction on fully automated-analyser Beckman Coulter AU 48. Whereas Glory science co, ELISA kit from the USA was used to measure the amount of human L-FABP in tissue fluids, e.g, (serum, plasma, and urine).
Standard concentration was taken by drawing standard curve on graph paper on the horizontal and vertical plan. The corresponding concentration was found according

to the sample OD value by the Sample curve and calculate the value of standard concentration and OD was obtained using standard curve with the help of straight-line regression equation. Data was entered in SPSS Latest version for the analyses. The data for age, L-FABP at 4 h, creatinine at preoperative, postoperative 0 h,4 h, 24 h and 48 h, was described by using mean±SD, if normally distributed and median (IQR) otherwise. AKI was described by using frequency and percentage at 24 h and 48 h. Comparison of L-FABP, between subjects developing AKI and without AKI was performed by using t-test if normally distributed and Mann Whitney U test otherwise. Shapiro Wilk test was used for knowing the normality of data. Receiver operating curve was used to define cut off of L-FABP to predict AKI and sensitivity, specificity and accuracy were described by using percentage with 95% confidence interval. *p*-value ≤0.05 was considered significant.

RESULTS

In the current study 88 children who underwent cardiac surgery were included. Among these 57 (64.8%) were males and 31 (35.2) were females with mean age of 5.7±3.6 years (Table-1). The mean serum creatinine levels started with 0.5±0.1 mg/dl at pre-op, were recorded as 0.6±0.1 at immediately post-op and remained same 24 hours after surgery (Table-2).As per criterion, 10 (11.4%) cases had postoperative increase in serum creatinine more than 0.3 mg/dl and therefore labelled as the group with acute kidney injury. When compared the median serum creatinine levels remained 0.6mg/dl (0.5–0.6) at post-op, 0.6mg/dl (0.6–0.7) at 4 hours, 0.8 mg/dl (0.7–0.8) at 24hours and 1.0 mg/dl (1.0–1.3) at 48 hours. For the group free of kidney injury, it remained 0.6 mg/dl (0.5–0.6) throughout. The difference at 4 hours was insignificantly with *p*-value 0.082 and at 24 and 48 hours with *p*-values <0.001 (Table-3).

Urinary LFABP levels were measured 4 hours after surgery and the mean level for AKI group was 310±86 ng/l with median levels 331ng/l (270–367) and that for NAKI was 204±60 ng/L with median levels of 190 (159–252). This difference was highly significant between two groups with *p*-value <0.001 (Table-4). Receiver operative characteristic curve was made for uLFABP level by taking AKI status on creatinine change criterion as gold standard. The area under the curve was 0.837 with a standard error of 0.082. The optimal cut off was found from this curve and it was 269 ng/L for ULFABP (Tabl-5, figure-1).

When this optimum point was used as a cut off, it was observed that 8/10 cases with AKI had their levels greater than 269 ng/L. Though 13 cases in NAKI also had levels greater than 269 ng/L. All other (65) cases had their uLFABP levels below 269 ng/L (Table-6). Based on this cut off the sensitivity of the marker at four hours to recognize AKI at later stage was found to be 80%, the specificity in this regard was 83.3%. The Positive predictive and negative predictive values were found to be 38.1% and 97.0% respectively with an accuracy level 83.0% (Table-7).

Table-1: Gender and age distribution of cases

Age	Gender		
	Male	Female	Total
Mean	6.0	5.3	5.7
Standard Deviation	3.6	3.6	3.6
Minimum	0.1	0.2	0.1
Maximum	11.7	11.9	11.9

Table-2: Serum creatinine level of cases before and after surgery at various times

Serum creatinine level	Pre–op	0 hours	4 hours	24 hours	48 hours
Mean(mg/dl)	0.5	0.6	0.6	0.6	0.6
Standard Deviation	0.1	0.1	0.1	0.1	0.2
Minimum	0.3	0.3	0.4	0.1	0.4
Maximum	0.8	0.9	0.8	1.3	1.4

Table-3: Serum creatinine levels for the cases with AKI n11 (11.4%) and without AKI. n78 (88.6%).

Serum creatinine level	Pre-op		Post-op		4 hours		24 hours		48 hours	
	AKI	NAKI	AKI	NAKI	AKI	NAKI	AKI	NAKI	AKI	NAKI
Mean (mg/dl)	0.5	0.5	0.5	0.6	0.6	0.6	0.8	0.6	1.1	0.6
Standard Deviation	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.2	0.1
Minimum	0.4	0.3	0.4	0.3	0.4	0.4	0.5	0.1	0.7	0.4
Median	0.6	0.5	0.6	0.5	0.6	0.6	0.8	0.5	1.0	0.6
Maximum	0.7	0.8	0.7	0.9	0.8	0.8	1.3	0.8	1.0	0.8
***p*-value**	0.853		0.956		0.081		0.001*		0.001*	

Mann Whitney, $p<0.005$ as significant.

Table-4: Urinary LFABP levels for cases with AKI n11 (11.4%) and without AKI n78(88.6%).

U LFABP level	AKI	NAKI	Total
Mean (ng/L)	310	204	216
Standard Deviation	86	60	72
Minimum	165	104	104
Median	331	190	194
Maximum	411	386	411
***p*-value**	0.001		

Table-5: Area under the ROC curve

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95 Confidence Interval	
			Lower Bound	Upper Bound
0.837	0.082	0.001	0.667	0.998

a. Under the nonparametric assumption b. Null hypothesis: true area = 0.5

Table-6: Status of cases by urinary LFABP levels at 4 hours against actual status of injury by creatinine level at 48 hours

U LFABP (ng/L) level	AKI		NAKI		Total	
	N	%	N	%	N	%
> 269	8	80.0	13	16.7	21	23.9
≤ 269	2	20.0	65	83.3	67	76.1
Total	10	100.0	78	100.0	88	100.0

Table-7: Predictive measures along 95% confidence interval for urinary LFABP levels at 4 hours against actual status of injury by creatinine level at 48 hours

Measure	Value (%)	95% Confidence interval
Sensitivity	80.0	55.2 – 104.8
Specificity	83.3	75.0 – 91.6
PPV	38.1	17.3 – 58.9
NPV	97.0	92.9 – 101.1
Accuracy	83.0	75.2 – 90.8

PPV=positive predictive values. NPV=negative predictive values

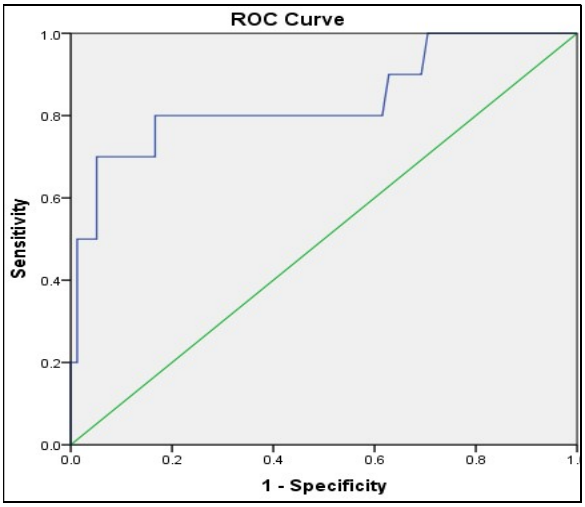

Figure-1: Receive operative characteristic (ROC) curve for urinary LFABP level to recognize acute kidney injury.

DISCUSSION

The current study was designed to assess the association of urinary L-FABP with AKI after cardiac surgery in paediatric patients. This study was performed on 88 paediatric patients with congenital heart disease who underwent cardiac surgery. According to age and gender from 88 patients, 57 (64.8%) were males and 31 (35.2%) were female with a median age of 5.0 (2.6–9.0) years. In comparison with this study, there is a study in which 27 paediatric patients were included with male to female percentage 15 (55.6%) and 12 (44.4%) with a median age of 360 days.[32]

In this study serum samples were obtained at five different intervals preoperative, postoperatively, oh and at 4, 24 and 48 hours after surgery for serum creatinine. The mean pre-op serum creatinine level was 0.5±0.1mg/dl and mean post-op to 24h were 0.6±0.1mg/dl. The mean serum creatinine levels at 48 hours were 0.6±0.2mg/dl and median and maximum levels were 0.6 mg/dl and 1.4 mg/dl. Consistent to this study, there is a study in which samples for serum creatinine were taken in five intervals, but the first post-op sample was taken at 2 hours[32]. In another study on adult's serum samples were obtained at seven different intervals from pre-op to 48 hours and the levels of serum creatinine were consistent with current study.[33]

AKI was established by taking creatinine levels as a gold standard, such as an absolute or abrupt increase in serum creatinine levels from 0.3mg/dl from the baseline within 48hours.[2] Based on this rise in serum creatinine, patients were distributed into two groups, i.e., AKI and non-AKI. In similar study, Matsui K[33] also

used this criterion for the establishment of AKI in adults, whereas Ivanisevic I[32], Krawczeski CD[34] and Portilla D[35] used criteria for the establishment of AKI by 50% increase in serum creatinine levels from the baseline after surgery. As per criteria, 11.4% cases develop AKI after cardiac surgery and when the two groups were compared for serum creatinine the difference was significant at 24 hours and 48-hours. As compared to other studies, the percentage of developing AKI after cardiac surgery is decease in this study whereas in other studies the percentage of developing AKI was 27–52 percent.[32–34]

A urine sample was taken 4 hours after cardiac surgery for the measurement of urinary L-FABP. The mean level of u L-FABP for the AKI group was 310±86 ng/l with median levels 331 (270–367) ng/l and for non-AKI, the mean levels were 204±60 ng/l with median levels of 190 (159–252) ng/l. The difference was highly significant between AKI group and non-AKI group. These results are consistent with Portilla D[35] who reported in his study that u L-FABP at 4 h after surgery in AKI group was highly significant than the non-AKI group but the urinary samples were taken at different intervals after surgery. In another study in which Krawczeski CD[34] measured uL-FABP at different time intervals and they found that uL-FABP at 6 and 12 hours after surgery were highly significant between AKI and non-AKI groups. In a study conducted by Ivanisevic I[32] they also measured uL-FABP at different time intervals and found that uL-FABP was significantly higher in AKI group than non-AKI group at 2,6 and 48 h after surgery.

In this study serum, creatinine levels were taken as a gold standard for the establishment of AKI and non-AKI at 48h than compared with uL-FABP at 4h. There are certain studies in which they have used creatinine levels for the establishment of AKI and non-AKI at 48h and then compared uL-FABP at different time intervals.[31,33]

Sensitivity and specificity of uL-FABP according to the cut-off and receiver operative curve was calculated. The receiver operative characteristic curve was made for u LFABP level by taking serum creatinine change criterion as the gold standard. The area under the curve and a standard error was as fellow 0.837 and 0.082. Under this curve, optimal cut-off was 269 ng/L for uL-FABP. Based on this cut-off values at 4 hours to recognize AKI the sensitivity of uLFABP were 80% and specificity 83.3% which indicates that uL-FABP is a good predictor for the diagnosis of AKI. Similar results were obtained in a study by Portilla D[35] where they measured uL-FABP before and after surgery on 40 paediatric patients in which uL-FABP levels were found to be an independent risk indicator at 4 hours after surgery with area under the receiver operating characteristic curve 0.810, sensitivity 0.714 and specificity 0.684.

In another study[35] measured uL-FABP at different time intervals prior to and after cardiac surgery on 220 paediatric patients in which at 6 hours area under the receiver operating characteristic curve was 0.73 which is a good indicator that uLFABP can be a useful marker for AKI. Ivanisevic I[32] measured uL-FABP at different time intervals before and after cardiac surgery on 27 paediatric patients in which at 2 hour, 6-hour area under the receiver operating characteristic curve was 0.867 with a cut-off at 2 hours was 450 µg/g creatinine with sensitivity and specificity 0.500 and 0.867 respectively and at 6 hours cut off uL-FABP was 250 µg/g creatinine with sensitivity and specificity of 0.667 and 0.900, respectively.

Concerning gender and age, no significance has been measured between AKI group and non-AKI group in this study. Similar results have been found in which there is no difference between AKI and non-AKI group with respect to gender and age.[31] The results are also consistent with another study with respect to gender and age[35] and in adults[33] also. In contrast to these studies, there is a study in which statistic value is not significant for gender but significant for.[34]

CONCLUSION

It may be concluded from this study that uL-FABP may be considered to act as early predictor for the development of AKI in paediatric patients undergoing cardiac surgery with 80% sensitivity and 82% specificity with an optimal cut-off value of 269 ng/L.

Limitations and future research

There were certain key limitations to this study. It was a single centre study with a relatively smaller sample size which may not be sufficient to estimate the uL-FABP levels and its association with AKI. Also, due to financial constraints, uL-FABP was measured only at 4 hours of surgery. A follow-up study of longer duration with larger sample size and with different time interval before and after cardiac surgery may show the precise changes in the levels of uL-FABP and may help to evaluate uL-FABP more accurately as a diagnostic marker of AKI. In further studies, different biomarkers such as uNGAL, KIM-1, IL- 18 and uL-FABP may be measured at a different time interval to evaluate AKI.

AUTHORS' CONTRIBUTION

MBK: Contribution to the design, concept, data acquisition, analysis and paper writing. TN: Drafting the work, critically revising. HDW: Data acquisition, analysis and paper writing. AA: Contribution to the study design and discussion writing. ABS: manuscript preparation and proof reading. RI: result analysis and final approved of the draft

REFERENCES

1. Dalal R, Bruss ZS, Sehdev JS. Physiology, Renal Blood Flow and Filtration. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.
2. Kdigo A. Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int 2012;2(Suppl 1):1–38.
3. Alejandro V, Scandling JD Jr, Sibley RK, Dafoe D, Alfrey E, Deen W. *et al*. Mechanisms of filtration failure during postischemic injury of the human kidney. A study of the reperfused renal allograft. J Clin Invest 1995;95(2):820–31.
4. Bonventre JV, Weinberg JM. Recent advances in the pathophysiology of ischemic acute renal failure. J Am Soc Nephrol 2003;14(8):2199–2210.
5. Schrier RW, Wang W. Acute renal failure and sepsis. N Engl J Med 2004;351(2):159–69.
6. Le Dorze M, Legrand M, Payen D, Ince C. The role of the microcirculation in acute kidney injury. Curr Opin Crit Care 2009;15(6):503–8.
7. Mason J, Torhorst J, Welsch J. Role of the medullary perfusion defect in the pathogenesis of ischemic renal failure. Kidney Int 1984;26(3):283–93.
8. Karlberg L, Norlen BJ, Ojteg G, Wolgast M. Impaired medullary circulation in postischemic acute renal failure. Acta Physiol Scand 1983;118(1):11–7.
9. Rabelink TJ, de Boer HC, van Zonneveld AJ. Endothelial activation and circulating markers of endothelial activation in kidney disease. Nat Rev Nephrol 2010;6(7):404–14.
10. Basile DP. The endothelial cell in ischemic acute kidney injury: implications for acute and chronic function. Kidney Int 2007;72(2):151–6.
11. Blantz RC, Deng A, Miracle CM, Thomson SC. Regulation of kidney function and metabolism:a question of supply and demand. Trans Am Clin Climatol Assoc 2007;118:23–43.
12. Brezis M 3rd, Rosen S. Hypoxia of the renal medulla its implications for disease. N Engl J Med. 1995;332(10):647–655.
13. Beeuwkes R, Bonventre JV. Tubular organization and vascular-tubular relations in the dog kidney. Am J Physiol 1975;229(3):695–713.
14. Bagnasco S, Good D, Balaban R, Burg M. Lactate production in isolated segments of the rat nephron. Am J Physiol 1985;248(4 pt 2):F522–6.
15. Lok CE, Austin PC, Wang H, Tu JV. Impact of renal insufficiency on short- and long- term outcomes after cardiac surgery. Am Heart J 2004;148(3):430–8.
16. Mishra J, Dent C, Tarabishi R, Mitsnefes MM, Ma Q, Kelly C, *et al*. Neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker for acute renal injury after cardiac surgery. Lancet 2005;365(9466):1231–8.
17. Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med 1998;104(4):343–8.
18. Lassnigg A, Schmidlin D, Mouhieddine M, Bachmann LM, Druml W, Bauer P, *et al*. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: a prospective cohort study. J Am Soc Nephrol 2004;15(6):1597–605.
19. Zappitelli M, Bernier PL, Saczkowski RS, Tchervenkov CI, Gottesman R, Dancea A, *et al*. A small post-operative rise in serum creatinine predicts acute kidney injury in children undergoing cardiac surgery. Kidney Int 2009;76(8):885–92.
20. Goldstein SL, Devarajan P. Acute kidney injury in childhood: should we be worried about progression to CKD? Pediatr Nephrol 2011;26(4):509–22.
21. Bellomo R, Kellum JA, Ronco C. Defining acute renal failure: physiological principles. Intensive Care Med 2004;30(1):33–7.
22. McMahon GM, Waikar SS. Biomarkers in nephrology: Core Curriculum 2013. Am J Kidney Dis 2013;62(1):165–78.
23. Yamamoto T, Noiri E, Ono Y, Doi K, Negishi K, Kamijo A, *et al*. Renal L-type fatty acid binding protein in acute ischemic injury. J Am Soc Nephrol 2007;18(11):2894–902.
24. Chmurzyńska A. The multigene family of fatty acid-binding proteins (FABPs): function, structure, and polymorphism. J Appl Genet 2006;47(1):39–48.
25. Michael DS. Digestion and absorption of dietary triglycerides. In: Leung Po Sing, editor. The gastrointestinal system: gastrointestinal, nutritional and hepatobiliary physiology. New York: E-Publishing Inc, 2014; p.160–78.
26. Sharma A, Yogavel M, Sharma A. Utility of anion and cation combinations for phasing of protein structures. J Struct Funct Genomics 2012;13(3):135–43.
27. Basile DP, Leonard EC, Beal AG, Schleuter D, Friedrich J. Persistent oxidative stress following renal ischemia–reperfusion injury increases ANG II hemodynamic and fibrotic activity. Am J Physiol Renal Physiol 2012;302(11):1494–502.
28. Mohamed Abd E, Lasheen NN. Comparative study on the protective role of vitamin C and L-arginine in experimental renal ischemia reperfusion in adult rats. Int J Physiol Pathophysiol Pharmacol 2014;6(3):153–65.
29. Kwiecien S, Jasons K, Magierowski M, Sliwowski Z, Pajdo R, Brzozowski B, *et al*. Lipid peroxidation, reactive oxygen species and antioxidatie factors in the pathogenesis of gastric mucosal lesions and mechanism of protection against oxidative stressindued gastric injury. J Physiol Pharmacol 2014;65(5):613–22.
30. Belcher JM, Garcia-Tsao G, Sanyal AJ, Thiessen-Philbrook H, Peixoto AJ, Perazella MA, *et al*. Urinary biomarkers and progression of AKI in patients with cirrhosis. Clin J Am Soc Nephrol 2014;9(11):1857–67.
31. Yang J, Choi HM, Seo MY, Lee JY, Kim K, Jun H, *et al*. Urine liver-type fatty acid binding protein predicts graft outcome up to 2 years after kidney transplantation. Transplant Proc 2014;46(2):376–80.
32. Ivanišević I, Peco-Antić A, Vuličević I, Hercog D, Milovanović V, Kotur-Stevuljević J, *et al*. L-FABP can be an early marker of acute kidney injury in children. Pediatr Nephrol 2013;28(6):963–9.
33. Matsui K, Kamijo IA, Sugaya T, Yasuda T, Kimura K. Usefulness of urinary biomarkers in early detection of acute kidney injury after cardiac surgery in adults. Circ J 2012;76(1):213–20.
34. Krawczeski CD, Goldstein SL, Woo JG, Wang Y, Piyaphanee N, Ma Q, *et al*. Temporal relationship, and predictive value of urinary acute kidney injury biomarkers after pediatric cardiopulmonary bypass. J Am Coll Cardiol 2011;58(22):2301–9.
35. Portilla D, Dent C, Sugaya T, Nagothu KK, Kundi I, Moore P, *et al*. Liver fatty acid binding protein as a biomarker of acute kidney injury after cardiac surgery. Kidney Int 2008;73(4):465–72.

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