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To Assess Urinary Glutathione- S- Transferase Isoenzymes in Identifying of Acute Kidney Injury Following Heart Surgery

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ABSTRACT:

BACKGROUND: Biological markers for acute kidney injury (AKI) have yet to be widely used in clinical practise, despite their promise of earlier detection and risk stratification. We measured urinary α and π glutathione S-transferases (α-GST and π-GST), glutathione S-transferase (GST) subtypes π and α as biomarkers of acute kidney injury (AKI) during heart surgery patients.GSTs' role in oxygen radical disposal and the pathogenesis of cardiac surgery and cardiopulmonary bypass (CPB)-associated AKI, as well as new insights into GSTs' site-specific expression in identified parts of the nephron during renal damage, are highlighted.

METHODS:This study at DMMC and SMHRCwanadongri Nagpur in collaboration with AVBRH sawangimeghewardha.80 subjects included in this research and divided in two groupsStudy group:40 subject AKI in after heart surgery and Control group: 40 subject healthy subjects.

RESULTS:α-GST increased in study group (20±2.03) as compared to control group (6.5±0.02) and urinary π-GST and serum creatinine level also increased in study group (16±0.09, 2.30±0.6) as compared to control group (13±0.06, 1.2±0.02).

In present study statistically both increase in urinary α-GST and urinary π-GST following adult heart surgery, but both α-GST and π-GST return to lower levels in 24 hrs.

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CONCLUSIONS: in the present research concluded patients data suggest a relation of urinary α-GST and π-GST in the early diagnostic evaluation of acute kidney injury (AKI) post heart surgery.

KEY WORDS:Urinary α-GST,Urinaryπ-GST, AKI, Heart Surgery.

INTRODUCTION:

In acute kidney injury (AKI) is linked to an increased risk of morbidity and mortality in the ICU patient and has clinical implications. The estimation of serum creatinine is still used in clinical diagnosis of acute kidney injury .[1,2]

Biomarkers of urinary glutathione-s-transferase (GST) family of protein have received relatively little consideration in the literature in acute kidney injury (AKI).[3,4]

The glutathione-s-transferase (GSTs) family of protein , which is classified into three major subtypes, α GST, π GST and μ GST is a ubiquitous enzyme that participates in free radical detoxification.Each isoenzyme is made up of two subunits, each of which is given a name based on their composition. GST proteins have been obtained from a wide range of human tissues (kidneys, liver, small intestines, testes, ovaries, and adrenal glands) and are well recognized.The human renal contains the α and π GST forms in relatively present in increased amounts in renal tubules.[5]

Weightof molecularα-form has a of 51 kDa and molecular weightof π-form 47 kDa. Urinary α-GST and π-GST are histologically established renal biomarkers with well-validated cellular origins that are crucial to their diagnostic understanding. The GST proteins in the nephron are specific site of the α-GST is form is mainly found in the proximal tubule, whereas the π-GST is found in the distal tubule.[5]Urinary α and π-GST are only increased in the during renal injury, producing them excellent early stages of renal tubular damage.[6]

GST proteins are phase II enzymes that catalyse the formation of reduced glutathione (GSH)-electrophile conjugates, which help in the detoxification of electrophilic compounds.[7]GSTs have been shown to play an important role in protecting cells from oxidant-mediated injury by catalysing the composition of lipid hydro peroxides produced by oxidative damage to cellular lipid molecules in several studies. [8,9]

GSTs can decrease the cytotoxicity of lipid peroxidation end-products like 4-HNE by detoxifying them with GSH conjugates.[9]By inactivating these reactive oxygen species, the GST proteins limit the toxic effects of oxidative intermediates on tubular cells and provide a physiological response to tubular cell injury. α and π-GST are preformed cellular proteins that are only increased during renal injury and can be identified within 1 hour of cardiopulmonary bypass (CPB).[10]

MATERIALS AND METHODS

Thispresent study was a case control study conducted in the department of biochemistry cardiology and nephrology of Datta MegheMedical College (DMMC) and shalinitaimeghehospital & research centre (SMHRC)wanadongri Nagpur and collaboration with AVBRH sawangimeghewardha.

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STUDY POPULATION:80 subjects included in this research and divided in two groups.

1. Study group:40 subject AKIin after heart surgery.
2. Control group: 40 subject healthy subjects.

DURATION OF STUDY: September 2020 to February 2021**.**

INCLUSION AND EXCLUSION CRITERIA:

Inclusion criteria:

patient suffering from AKI after heart surgery.

Exclusion criteria:

Subject suffering from mycobacterium tuberculosis, HIV,HbsAg etc.

BLOOD SAMPLE COLLECTION: 3ml blood was collected in plain vial for the serum separation from each subject by venipuncture with standard blood collection technique.

URINE SAMPLE COLLECTION:3mlurine sample was collected in sterile container for the estimation of urinary glutathione-s- transferase.

BIOCHEMICAL ANALYSIS:

- Estimation of serum creatinine was estimated by jaffe's method.
- Estimation of urinary α and π-GST was estimated by ELISA method.

STATISTICAL ANALYSIS:

The SPSS software programmed, version 20.0, was used to analyse the data. The standard deviation and mean were calculated. Using descriptive and inferential statistics, the data was analyses and interpreted. It was considered statistically acceptable since the probability value was less than 0.05 ($p<0.05$).

RESULT:

Table NO: 01 show the post-operative urinary*α*-GST, *π*-GST and serum creatinine level in study group and control group.

Parameter	Study group	Control group
α-GST	201.3±81.5	6.5±0.02
π-GST	27.6±15.6	13±0.06
Serum creatinine	2.10±0.5	1.2±0.02

Table no 01 show the α-GST increased in study group (201.3±81.5) as compared to control group (6.5±0.02). and urinary π-GST and serum creatinine level also increased in study group (27.6±15.6, 2.10±0.5) as compared to control group (13±0.06, 1.2±0.02)

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Table NO: 02 show the urinaryα-GST, π-GST, and serum creatinine level in after 24 hrs

Parameter	Study group	Control group
α-GST	20±2.03	6.5±0.02
π-GST	16±0.09	13±0.06
Serum creatinine	2.30±0.6	1.2±0.02

Table no 02 show the α-GST increased in study group (20±2.03) as compared to control group (6.5±0.02) and urinary π-GST and serum creatinine level also increased in study group (16±0.09, 2.30±0.6) as compared to control group (13±0.06, 1.2±0.02).

In the current study, there was a statistically significant increase in both urinary α-GST and urinary π-GST following adult heart surgery, but both returned to lower levels before 24hrs.

DISCUSSION:

The glutathione S-transferase (GST) family of proteins has received relatively little attention in the literature, despite recent articles and research on biomarkers in acute kidney injury.[3,4]

GST tests have been used in a number of heart surgery intervention studies, and a few that used hydroxyethyl starch (HES) preparations.[11,12,13.]

α-and,π-GST excretion, as well as the excretion of other tubular enzymes, could be used as biological markers for subclinical renal damage undergoing cardiopulmonary bypass.[14]

Urinary π-GST and neutrophil gelatinase-associated lipocalin (NGAL) concentrations in the albumin group were significantly higher than in the HES group immediately after surgery and 5 hours later in the ICU, likely indicating subclinical renal tubular injury, with no significant difference in serum creatinine levels. As a result, urinary concentrations of α-GST may be more responsive and accurate than serum creatinine, a glomerular function marker, in assessing the impact of volume substitution strategies on tubular integrity.This is backed up by research showing that patients undergoing on-pump coronary artery bypass surgery have higher urinary α-GST levels than those undergoing off-pump surgery.[15,16.]

Association of cardiopulmonary bypass with acute kidney injury in heart surgery.[17]

In present researchTable no 01 show the α-GST increased in study group (201.3±81.5) as compared to control group (6.5±0.02). and urinary π-GST and serum creatinine level also increased in study group (27.6±15.6, 2.10±0.5) as compared to control group (13±0.06, 1.2±0.02) and table no 02 show the α-GST increased in study group (20±2.03) as compared to control group (6.5±0.02) and urinary π-GST and serum creatinine level also increased in study group (16±0.09, 2.30±0.6) as compared to control group (13±0.06, 1.2±0.02).

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In the current study, there was a statistically significant increase in both urinaryα- and urinary π-GST following adult heart surgery, but both returned to lower levels within 24hrs. The **Eijkenboom et al.**[18]assess the diagnostic accuracy of urinary GSTs in the early detection of AKI (defined as a 50% or 0.3 mg/dl increase in serum creatinine from baseline) following elective heart surgery. Based on the pattern of urinary GST enzyme excretion, they also tried to figure out where tubular injury occurred. However, only one patient in the study's 84 participants had AKI.The researcher showed a small but statistically significant increase in urinary α and π-GST after adult cardiac surgery, but both appeared to return to normal levels after 24 hours.

According to the authors, this temporary increase in GST protein excretion had no correlation with changes in serum creatinine and did not predict clinically significant changes in renal function. However, since clinical AKI is uncommon in this patient group, it's difficult to draw any conclusions about GSTs' diagnostic success in predicting AKI after heart surgery, including the possibility that transient postoperative urinary GST increases may indicate subclinical renal tubular injury (without a rise in serum creatinine) and/or a tubular response to oxidant stress.

McMahon BA et al.[19] Urinary α-GST and π-GST can also assist in the diagnosis of heart surgery-related AKI, according to the show. In the postoperative phase, both urinary α-GST and π -GST are observed.At the time of the initial diagnosis of AKI, π-GST was the best predictor of AKI severity. α-GST was able to foresee the progression of both stage 1 and stage 3 AKI in the future.

CONCLUSION:

In conclusion in the present research patients of small data suggest a role of urinary α and π-GST in the early diagnostic increased ofacute kidney injury (AKI) post heart surgery. The continued production of urinary α-GST and π-GST for this reason will involve comparison with other novel markers of AKI. In medical practice, urinary α-GST and π-GST have some potential to detect AKI in heart surgery and other risk AKI.

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