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EFFECT OF GRAM NEGATIVE BACTERIA INFECTION ON RENAL AND LIVER FUNCTION

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ABSTRACT

In a tropical country like India, particularly in Tamilnadu, infection by gram negative bacteria is quite common and the four commonly infecting gram negative bacterias are *Klebsiella, Pseudomonas, Enterobacter and Escherichia coli*. Numerous studies done previously have indicated that infections by gram negative bacteria affects all vital organs, particularly liver and kidney. The aim of this study was to find out the effect of gram negative bacteria on renal and liver functions. This study was carried out with a reasonable number of patients (total 67) involving both sexes in each type of infection. Our aim was to find out the effect of infection by gram negative bacteria on renal and liver functions. It has been shown that both the organs are affected during such infections as per alterations observed in the biochemical analytes associated with the organs. While *Klebsiella, Ecoli and Enterobacter* affect both liver and renal functions, *Pseudomonas* affect only liver functions as per statistical analysis presented in this paper.

KEYWORDS: *Klebsiella, Pseudomonas, Enterobacter, Escherichia Coli,* Urea, Creatinine, ALT.

INTRODUCTION

Infectious diseases are still dominating in developing countries and environment plays a major role in the transmission of vector-born infectious diseases such as malaria, dengue, Kala azar, Filarasis and Chikungunya to name a few. Each year infectious diseases kill approximately 3.5 million people worldwide affecting mostly the poor and young children who live in low and middle income countries. Although biochemical alterations have been extensively studied in many of the common infections, studies related to infection by *E. Coli, Klebsiella, Pseudomonas and Enterobacter* are lacking. Research can change this and bring health to many more. The poorest in developing countries face a burden of communicable diseases. Disease that has re-emerged may be due to evolution of antimicrobial resistance by pathogens or due to insecticidal resistance by vector, human migration, HIV/AIDS and changes in transmission strategies. The aim of this study is to evaluate the alternations in biochemical analytes related to renal and liver due to infections caused by *Escherichia coli* ***(****E. Coli), Klebsiella, Pseudomonas and Enterobacter* gram negative bacteria

Escherichia coli

E. coli + bile peritonitis rats had significantly elevated levels of bilirubin, Alkaline Phosphatase (ALP), Aspartate transaminase (AST) and Alanine transaminase (ALT) as compared with both controls and rats with peritonitis induced by E. coli alone. Hepatic dysfunction as revealed by routine laboratory tests is seen early in experimental peritonitis in the rat, but this is not accompanied by a reduced antipyrine clearance rate.[1] There was an increase in the number of E. coli in the proximal small intestinal flora in Nonalcoholic Steatohepatitis (NASH) group than in control group and Tumor necrosis factor- α (TNF-α) level was significantly higher in NASH group than in control group.[2] Serum Procalcitonin (PCT), and C-reactive protein (CRP) levels were used in differentiating sepsis from systemic inflammatory response syndrome (SIRS), identifying new fever caused by bacteremia, and assessing prognosis when new fever occurred. On Intensive Care Unit (ICU) day 1, the sepsis group had higher serum soluble triggering receptor expressed on myeloid cells 1 (sTREM-1), PCT, and CRP levels compared with the SIRS group.[3] Although CRP levels are reduced in response to acute infection, production is nevertheless maintained even in patients with advanced liver dysfunction.[4]

Klebsiella

The most common predisposing factors associated with *Klebsiella pneumonia* (K pneumoniae) were diabetes mellitus (58%), urolithiasis (25%) and immunosuppression (17%). All patients with *K pneumoniae* and renal abscesses should receive empiric antibiotics and percutaneous drainage or aspiration, and surgical intervention as necessary for patients with intractable disease.[5] In *K pneumonia* laboratory data showed raised enzyme levels of ALT, ALP, AST, increased direct bilirubin and White Blood Corpuscles (WBC) count 10.6 K/µl with neutrophilia.[6] *K pneumoniae* bacteremia was commonly associated with elevated liver enzymes (12 of 18), whereas none of the infants with Pseudomonas aeruginosa bacteremia had elevated liver enzymes. Gram-negative bacteremia is commonly associated with cholestasis in premature neonates. Liver enzyme abnormalities are more common than elevated conjugated bilirubin, not all gram-negative bacteria have the same effect and the lack of enteral feeding seems to play a more significant role than the administration of parenteral nutrition.[7]

Myocarditis is an uncommon disease that presents with a wide range of symptoms in children and adults. It is histologically characterized by varying degrees of myocardial necrosis, oedema and cellular infiltration. Myocardial inflammation is a nonspecific response to many triggers such as bacterial infection, cardio toxic agents, or mechanical injury. All biochemical analyses showed statistically significant increase in the measured parameters due to bacterial infections except for blood urea which appear to be normal. A significant positive correlation was observed between LDH with creatinine. In the 7 days group, there were significant positive correlations between AST and ALT, Erythrocyte Sedimentation Rate (ESR) with Urea and ALP with CRP. Many of these biomarkers will provide important new insights into pathophysiology and aid in the diagnosis and management of cardiovascular patients.[8] An increased frequency of infections has been reported in patients with chronic liver disease. The tendency of patients in this population to acquire Urinary Tract Infection (UTI) is not completely understood. A significantly greater number of UTIs are observed in patients with biliary atresia than in those without it.[9]

Enterobacter

Many bacteria among the *Enterobacter* genus are involved in infectious diseases and diarrhoea. Significant increase of some biochemical parameters such as AST, ALT, ALP and creatinine were found.[10] Patients with biochemical evidence of liver disease generate

significantly lower serum CRP concentrations during bacteraemia than patients without liver dysfunction. Serum CRP concentrations should be interpreted with caution in patients with liver disease to diagnose and monitor bacterial sepsis.[11]

Pseudomonas

Histological findings of the liver included cholestasis, Kuepfer cell hyperplasia and cell infiltration in the sinusoid and portal areas, however these findings were mild and nonspecific. It is important to recognize the presence of hyperbilirubinemia associated with sepsis in order to properly treat febrile elderly patients with hyperbilirubinemia.[12] Although CRP levels are reduced in response to acute infection, production is nevertheless maintained even in patients with advanced liver dysfunction.[13] Decreased metabolic activity of liver cells associated with bacteremia, probably leading to impaired bilirubin excretion. Patients died despite appropriate antibiotic therapy. Isolated hyperbilirubinemia, thus, seemed to be an ominous prognostic sign in severe infection.[14]

MATERIAL AND METHODS

A total of 67 gram negative bacteria infected patients in the age group of 9 – 75 years (Males & Females) who were investigated for blood culture and other routine biochemical, haematological parameters and liver and renal function tests were enrolled for this study. Out of the 67 gram negative bacteria infected patients, 20 patients each were positive for *Klebsiella* and *E. coil* infection,*13* were for *Pseudomonas* and 14 for *Enterobacter* infection. The sole aim of this study was to find out the effect of infection by gram negative bacteria on Liver and renal function.

Inclusion Criteria

- All patients in the age group of 9 to75 years, both Male and Females
- Patients who do not have previous history of kidney and Liver diseases
- Patients who were diagnosed to have Infection due to bacteria like *Klebsiella, Pseudomonas, Enterobacter, E.Coli.*

Exclusion Criteria

- Patients with previous history of Renal and Liver diseases.
- Patients who were not diagnosed to have Infection due to bacteria *like Klebsiella, Pseudomonas, Enterobacter, E.Coli.*
- Patients having chronic illness.

Dirui CS 1300 analyser and Dialab reagents were used to measure all the biochemical analytes. The accuracy of all biochemical tests done for this study was validated by the use of Bio-Rad accuracy controls at two levels. For statistical analysis of data, a software downloaded from the website http://www.vassarstats.net was used to calculate correlation coefficient (r), students 't' distribution (t) and probability (p) between two tests for normal and abnormal renal and liver function test groups.

RESULTS

Table I: Statistical Analysis (r, t & p) for *Klebsiella* (K) infection (n=20)

Analytes Compared	r	t	P
UREA N VS K	-0.3406	-1.5370	0.0709
TP N VS K	-0.7131	-4.3150	0.0002
ALB N VS K	-0.3060	-1.3640	0.0947
ESR N VS K	-0.3804	-1.7450	0.0490

Table II: Statistical Analysis (r, t & p) for *E.Coli* infection (n=20)

Analytes Compared	r	t	p
UREA N Vs *E.coli*	-0.3526	-1.599	0.0636
GGTP NVs *E.coli*	0.3462	1.566	0.067
WBC N Vs *E.coli*	0.5195	2.579	0.0094

Table III: Statistical Analysis (r, t & p) for *Enterobacter* (Eb) infection (n=14)

Analytes Compared	r	t	p
UREA N Vs Eb	-0.4099	-1.557	0.0727
CREAT N Vs Eb	-0.4900	-1.947	0.0376
TP N Vs Eb	0.3877	1.457	0.085
ALB N Vs Eb	0.7148	3.541	0.002

Table IV: Statistical Analysis (r, t & p) for *Pseudomonas* (P) infection (n=13)

Analytes Compared	r	t	p
TB N Vs P	-0.4073	-1.479	0.084
DB N Vs P	-0.3928	-1.417	0.092
GGTP N Vs P	-0.4518	-1.68	0.061

Table I to IV presents the statistical parameters viz r, t and p values for liver and renal function tests done in each group of infected patients. Significant inverse correlations were observed between the normal group and *Klebsiella* infected patients for urea, proteins, albumin and ESR, the highest for Total proteins indicating that both renal and liver functions are affected during infection by *Klebsiella*.

In *E. Coli* and *Enterobacter* infections too, tests such as urea, GGTP as well as urea, creatinine & A/G ratio are altered as shown in Tables II and III. However, only liver function is affected in the case of *Pseduomonas* infections as observed by the association observed bilirubins and GGTP in Table IV. Positive correlations were observed between GGTP and WBC in the case of *E. Coli* infection and Total proteins and albumin in *Enterobacter* infections.

From the statistical data shown in all the 4 Tables it is clear that some correlations were found between the types of bacterial infections and some biochemical analytes related to Kidney and Liver functions. Some recent studies have linked bacteremia to cardiac functions and hence this study could be extended to cardiac patients also.

DISCUSSIONS

Many previous studies have shown alterations in the functioning of both renal and liver due to infections caused by gram negative bacteria among which *Klebsiella, Pseudomonas, Enterobacter and E.Coli* are prominent. It has been show that during *E.Coli* infections inflammatory markers PCT and CRP were altered but we could not do these analytes as we wanted to link only routine biochemical analytes related to renal and liver functions to gram negative bacterial infection.[4] In our study we could indeed prove that majority of analytes related to kidney and liver are altered due to such infections.

In an earlier study it has been shown that all liver function tests such as ALP, ALT, AST showed an association in *Klebsiella* infections.[7] but we could prove only urea, TP, albumin and ESR showing correlation and clearly establishing the involvement of renal as an additional organ getting affected. Similar observations are found out in the case of *Enterobacter*.[11] As in the case of *E.coli*, we have proved that Pseudomonas infection will certainly alter the functions of liver as per our observations of alterations in Bilirubin and GGTP values. Hence our study has proved that the four gram negative bacteria studied will indeed affect both renal and liver functions. In a study related to infection by pseudomonas, they have proved that only inflammatory markers PCT and CRP are altered but our study has proved that liver function is affected in such infections.[12]

CONCLUSION

This study done with the least budget and using a reasonable number of patients infected with gram negative bacteria has linked such types of infections to alterations in

biochemical functions of both liver and Kidney. Statistical analysis done clearly demonstrated that some principal analytes involved both in liver and kidney are altered during such infections as shown by inverse correlations observed for analytes like urea, TP, Albumin, GGTP & Bilirubin there by linking laboratory diagnosis of clinical microbiology to biochemistry. The contents of this paper will help research scholars to undertake such works covering large number of gram negative infected patients and to recommend a list of biochemical tests as routine investigations for the laboratory diagnosis of such patients.

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