



Raised Serum Creatinine in *Klebsiella Pneumoniae* Pulmonary Infection Probably Owes to Nitrogen Fixation

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ABSTRACT

Klebsiella pneumoniae is a nitrogen fixing bacteria which is prevalent with pulmonary infection. Creatine is naturally produced in human body which is metabolic waste. When nitrogen content is more in the body this leads to more amino acid synthesis finally increase the level of creatinine. We selected 27 patients who were suffering from *K. pneumoniae* infection in the lungs as case group and 27 patients who were suffering from *Pseudomonas aeruginosa* infection in the lungs as control group. There was no evidence of factors which raised serum creatinine levels in these selected patients. Serum creatinine levels were estimated on the days of receiving clinical samples (sputum/ broncho alveolar lavage fluid endotracheal aspirate) which gave positive cultures of the above mentioned microorganisms were accepted for further analysis and patients were also selected accordingly. The mean serum creatinine level of *K. pneumoniae* infected group was found to be 1.176 mg/dL while creatinine level of *P. aeruginosa* infected group was 1.062 mg/dL. The difference between two mean values of Serum creatinine levels in the two groups was found to be highly significant at 0.001 level. Thus it may be concluded that nitrogen fixation indirectly occurs in human body with *K. pneumoniae* infection.

KEYWORDS: Nitrogen fixation; Creatinine; *Klebsiella pneumoniae*

INTRODUCTION

Although Earth's atmosphere contains abundant nitrogen, animals together with human beings and plants could not exploit it while a small number of microbes can fix it. Several microbes pathogenic to human beings confirmed their skill of this distinctive nitrogen fixing activity. One key associate of this assembly - *Klebsiella pneumoniae* naturally occurs in the soil and about 30% of strains can fix nitrogen, which has been elaborately studied as free living diazotroph. *K. pneumoniae* is well known to produce bronchopneumonia and bronchitis in human beings affecting mostly the patient population with respiratory host defenses. Among diverse tests regularly done with blood of human beings to recognize protein catabolism status, serum creatinine is probably the most important one, although it is mainly utilized to know kidney excretory condition. Thus with normal kidney function a mildly increased serum creatinine level in pulmonary *K. pneumoniae* infected person may be due to Nitrogen Fixation. Creatine is naturally produced in the human body from amino acids like L-Arginine, Glycine and L-Methionine primarily in kidney and liver and after production, approximately 95% of it, is accumulated in skeletal muscle for utilization. The mitochondrial enzyme GATM (L-Arginine: Glycine) amidino transferases (AGAT, E C 2.1.4.1)

which play the key role in formation of creatinine is responsible for catalyzing the first rate limiting step of creatine biosynthesis. The second enzyme in this pathway is GAMT (Guanidinoacetate N-methyl transferases, (EC 2.1.1.2). Activities of both the enzyme are accentuated with increased amount of nitrogenous compound pool in the blood. Thus there is possibility that increased Nitrogen content in the body may lead to more synthesis of amino acids resulting increased creatinine level in the blood. Creatine is a metabolic waste of muscle transported through blood stream and filtered by kidney. There are also evidences that in patients suffering from *Klebsiella* septicemia with pneumonia, creatinine level in the most important risk factor associated with in-hospital mortality [1]. In an experiment in mice, it has been noticed that in *Klebsiella pneumoniae* infection serum creatinine was significantly increased (28.8 verses 11.0 $\mu\text{mol/liter}$, P value <0.01 compare to those in normal uninfected mice), while after infection with *Streptococcus pneumoniae* serum creatinine level was unchanged [2]. These findings also indirectly indicate that there is a possibility of nitrogen fixation by *K. pneumoniae* within human body in these conditions. Thus this study was done to look into what happens in human body serum creatinine when infections caused by these organisms occur in the lungs where they may persist with contact of atmospheric nitrogen.

MATERIALS AND METHODS

We selected 27 patients who were suffering from *K. pneumoniae* infection in the lungs and 27 patients who were suffering from *Pseudomonas aeruginosa* infection in the lungs. Only patients with serum creatinine levels less than 1.5 mg/dL and without any obvious evidence of any renal diseases were included in the study. *P. aeruginosa* infected group was considered as control group as this bacteria cannot fix nitrogen although there are evidences that a few *Pseudomonas* spp. can fix nitrogen. In *K. pneumoniae* infected group there were 23 males and 4 females and their ages were ranged from 48 to 92 years. Similarly in *P. aeruginosa* infected group there were 22 males and 5 females and their ages were ranged from 23 to 93 years. All the patients were with intravenous fluid therapy. Serum creatinine levels were observed on the days of receiving clinical samples (sputum/ broncho

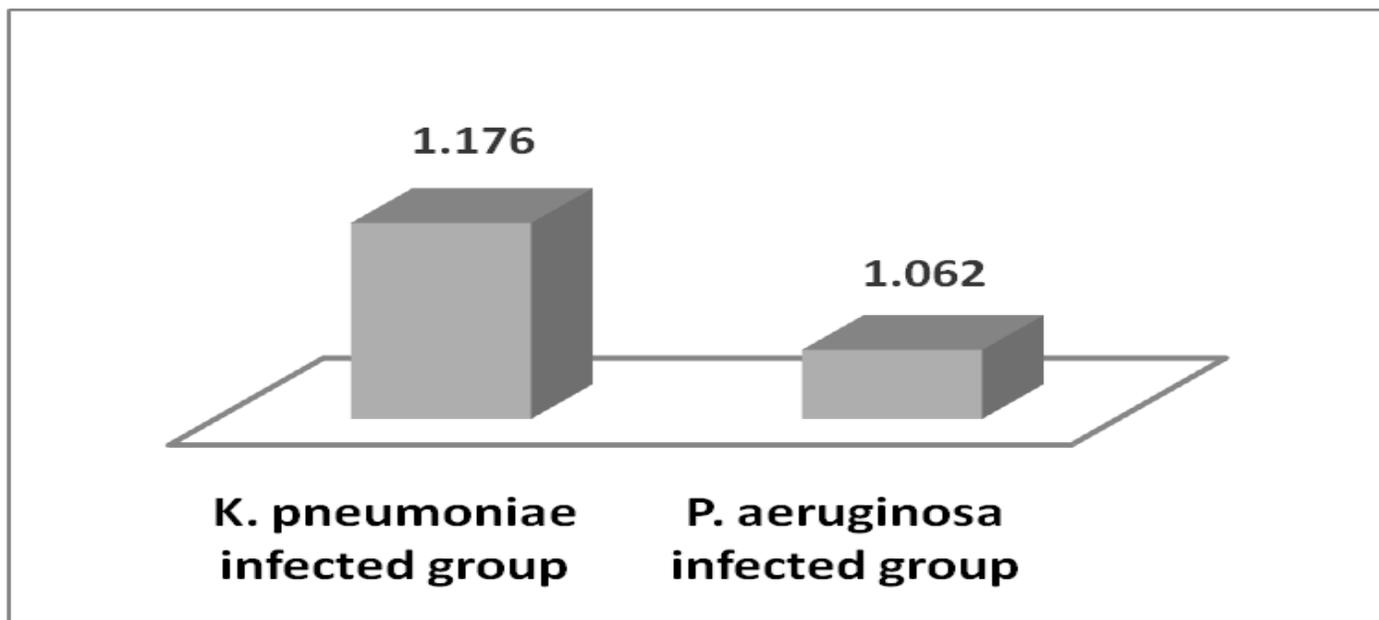
alveolar lavage fluid / endotracheal aspirate) which gave positive cultures of the above mentioned microorganisms were accepted for further analysis and patients were also selected accordingly. After collection of serum samples, creatinine levels were measured and analyzed to find out whether there were significant differences of serum creatinine levels in patients suffering from *K. pneumoniae* lung infection and *P. aeruginosa* pulmonary infections.

RESULTS

The results are given in the table and in the graph. The mean serum creatinine level of *K. pneumoniae* infected group was 1.176 mg/dL and the mean serum creatinine level of *P. aeruginosa* infected group was 1.062 mg/dL. Statistical analysis showed a t-value of the difference between two mean serum creatinine levels was 12.69 which was observed to be highly significant at 0.001 level.

	Mean (mg/dL)	Standard deviation (±mg/dL)	Standard error of Mean (±mg/dL)	
<i>K. pneumoniae</i> infected group	1.176	0.255	0.042	t-value of the difference is 12.69 (significant at 0.001 level)
<i>P. aeruginosa</i> infected group	1.062	0.349	0.058	

Table: Serum creatinine levels of *K. pneumoniae* infected group and *P. aeruginosa* infected group.



Graph 1: Mean serum creatinine levels of *K. pneumoniae* infected group and *P. aeruginosa* infected group.

DISCUSSION:

Nitrogen fixation in *K. pneumoniae* is a high energy consuming process and it depends on signals of molecular oxygen and ammonium availability [3,4,5,6]. Thus the regulation of the nitrogen fixation (*nif*) genes is very strict and this is mediated mainly by the products of *nifLA* operon. Activation of RNA polymerase by this regulatory systems is the key method of nitrogen fixation in *K. pneumoniae* in rejoinder to environmental signals [7,8](Grabbe and Schmitz, 2003; Klopprogge et al, 2002)[4]. Nitrogen is abundant in atmosphere and is converted into various forms like nitrous acid, nitric acid, ammonia. Amino acids are incorporated in proteins which make up the nucleic acid -the basic form of life. The conversion of this nitrogen occurs easily in certain bacteria like azotobacter found in leguminous plants. *K. pneumoniae* is a soil bacteria which can also fix nitrogen thus when it infects human body it can fix nitrogen which is reflected in the serum creatinine level. We have selected cases to exclude other factors influencing serum creatinine level. Thus it may be concluded that nitrogen fixation indirectly occurs in human body with *K. pneumoniae* infection.

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