Prevalence Of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospital

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Article ID: WMC001464
Article Type: Original Articles
Submitted on: 10-Jan-2011, 06:18:39 AM GMT Published on: 10-Jan-2011, 01:17:50 PM GMT
Article URL: article_view/1464
Subject Categories: MICROBIOLOGY
Keywords: Urinary Tract Infection; Nonfermenters; Pseudomonas spp.

How to cite the article: KL S, Rao G G, Kukkamalla A M. Prevalence Of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospital. WebmedCentral MICROBIOLOGY 2011;2(1):WMC001464

Source(s) of Funding:
Manipal university, Manipal

Competing Interests:
No competing interests
Prevalence Of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospital

Abstract

Background and Objective: Aerobic nonfermenting gram-negative bacilli (non-fermenters) are now emerging as important uropathogens. This study was done to know the prevalence of non-fermenters in Urinary Tract Infections (UTI) along with their antibiotic sensitivity.

Method: 5436 mid stream urine specimens received in six months period from July to December 2007 were subjected to Gram's staining, semi-quantitative culture, biochemical tests and antibiotic sensitivity testing as per the standard procedures in the routine microbiology laboratory and the results were noted.

Results: Out of the 1271 culture positive cases with significant bactereuria, 120 (9.44%) were caused by non-fermenters. Among the non-fermenters, Pseudomonas spp. was the most common (80.84%) followed by Acinetobacter spp. (19.16%). Majority of patients belonged to the age group of 15 to 50 years and most of them were females. Antibiotic sensitivity testing revealed that, among Pseudomonas spp., 75.25% isolates were sensitive to Piperacillin, 71.13% sensitive to Ciprofloxacin, 31.95% sensitive to Ceftazidime and 91.66% sensitive to Imipenem. In the case of Acinetobacter spp., 73.91% isolates were sensitive to Amikacin, 34.78% sensitive to Norfloxacin and all were sensitive to Imipenem. Out of the 18 non-fermenter isolates which were resistant to commonly used antibiotics, 15 were from inpatients indicating the possibility of nosocomial infection.

Conclusion: The non-fermenters are emerging as important cause of Urinary Tract Infections. In this study, Pseudomonas spp. was the most common non-fermenter isolated in significant numbers in MSU specimens. But, Acinetobacter spp. appeared to be more resistant to in vitro antibiotics in general.

Introduction

Urinary tract infections (UTI) are the second most common bacterial infections affecting humans throughout their lifetime. They are frequent cause of morbidity in outpatients as well as most frequent cause of nosocomial infection in many hospitals (Sussman M 1998) (9). Escherichia coli is the commonest urinary pathogen accounting for over 80% of community-acquired infection. Far less commonly Klebsiella spp., Proteus spp and Staphylococcus saprophyticus are responsible for community-acquired infection. The distribution of urinary pathogens in hospitalized patients is different with Escherichia coli accounting for about 50% of infections. Enterococcus, Klebsiella, Enterobacter, Citrobacter, Serratia, Pseudomonas aeruginosa, Providencia, and Staphylococcus epidermidis account for most of the rest. (Bryan et al 1984) (1). Aerobic nonfermenting gram-negative bacilli (nonfermenters) are a heterogeneous group of organisms that are either incapable of utilizing carbohydrates as a source of energy or degrade them via oxidative rather than fermentative pathway. (Koneman EWet al 1988) (4) This group includes organisms from diverse genera like Pseudomonas, Acinetobacter, Alcaligenes, Flavobacter, Oligella, Flavimonas, Agrobacter Weeksiella, etc. These organisms are common inhabitants of soil and water. They also exist as harmless parasites on the mucus membranes of humans and animals. Though primarily regarded as contaminants or incidental organisms, they are becoming increasingly important as opportunistic pathogens in immunocompromised patients. They can also cause infection by gaining access to normally sterile body sites through trauma. (Baron E.J et al 1990) (2). Though these organisms vary in their potential to cause infection and antibiotic susceptibility, there are common disease manifestations and risk factors. These organisms have been implicated in causing septicemia, meningitis, osteomyelitis, wound infections, pneumonia and urinary tract infections. Risk factors include immunosuppression, trauma, foreign body, broad-spectrum antibiotic use, infused body fluids like saline irrigations (Hall G.S1995) (3) and also urinary catheterization (Katsumi Shigemura 2006) (13). Pseudomonas aeruginosa is the predominant and most well known organism out of this heterogeneous group (Katsumi Shigemura et al 2006) (13) (Jombo G.T.A et al 2008) (14). This is partly due to its easy
recognition in the laboratory as it produces pyocyanin, a blue-green pigment. Other organisms usually get ignored as contaminants because identification up to species level is cumbersome and laborious and not possible in a busy routine microbiology laboratory (Stansfeld JM 1966) (8). It has been noted that the non-fermenter gram negative bacilli are being increasingly isolated in significant bacteriuria cases in routine urinary microbiology over the years indicating their potential in causing urinary tract infections. It is also well-known that most of these non-fermenter gram negative bacilli are resistant to many commonly used antibiotics for treatment (Gupta V et al 2002) (10) (Jamal W et al 2009) (11) (Nenek A et al 2008) (12) (Takeyama K et al 2008) (15). Evaluation of significance of isolating these organisms is complicated by the fact that they are usually present in mixed culture and the clinicians are rather unfamiliar with their names. This retrospective study was done to know the prevalence of nonfermenters in UTI along with their antibiotic susceptibility.

Materials & Methods:

Mid stream urine (MSU) specimens collected from both inpatients and outpatients attending Kasturba Hospital, Manipal (1500 bed capacity) for routine culture and sensitivity test, from July to December 2007 were included in this study. These MSU specimens were studied for significant bactereuria by gram staining and culturing on blood agar and MacConkey agar according to Kass concept (Hall GS et al 1995) (9). Those urine specimens containing organisms and pus cells on grams staining and yielding a pure culture of $10^5$ or more CFU/ml are considered to be significant bactereuria cases. They were further proceeded for species identification by standard biochemical tests. (Rambaugh KP et al 1999) (7) In-vitro antibiotic sensitivity test was performed by Kirby Bauer’s disc diffusion method using Muller Hinton Agar as per Clinical Laboratory Standards Institute (CLSI) guidelines and susceptibility pattern was noted. (Quinn PJ 1988) (10) In this study, we have included only the non-fermenters causing UTI. First and second line antibiotics used for oxidase positive non-fermenters were gentamicin (10 µg), tobramycin (10 µg), netilmicin (30 µg), amikacin (30 µg), ciprofloxacin (5 µg), ceftazidime & piperacillin (100 µg), where as for oxidase negative non-fermenters gentamycin(10 µg), netilmicin(30 µg), amikacin(30 µg), norfloxacin (10 µg), amoxicillin-clavulanic acid(10 µg), cefuroxime(30 µg) & cefotaxime(30 µg). Isolates resistant for all first & second line antibiotics were tested against third line antibiotics which included aztreonam(30 µg), cefpirome(30 µg), ticarcillin-clavulanic acid(30 µg), piperacillin-tazobactam (30 µg), cefoperazone-sulbactum & imipenem(30 µg) for both oxidase positive & negative non-fermenters. All culture media and antibiotic discs were from Himedia Laboratories Pvt Ltd, Mumbai, India.

Results

Out of the five thousand three hundred and forty six MSU specimens, no significant growth was recorded in four thousand seventy five (76.22%) specimens where as one thousand two hundred seventy one (23.38%) specimens showed significant growth. This indicates that approximately ¼ of the total specimens are significant bactereuria cases. Out of 1271 urinary isolates with significant bactereuria, number of fermenter gram negative bacilli was 1033 (81.27%), non-fermenters gram negative bacilli was 120 (9.44%), gram positive cocci was 81 (6.37%) and yeasts 37 (2.91%). Thus fermenter GNBs caused more than ¾ cases of significant bactereuria where as the remaining ¼ cases were caused by non-fermenter GNBs, GPCs and yeasts. In case of non-fermenter GNBs, the number of Pseudomonas spp. was 97 (07.63 %) and Acinetobacter spp. 23 (01.80 %). Illustrations 1 and 2.

Discussion and conclusion

Urinary tract infections are found in all age groups. The incidence is higher in male infants due to presence of congenital anomalies (Stansfeld J.M 1966) (9). From adulthood to the age group of 65 years, the incidence of UTI is very high in women as compared to men. In older patients there is a progressive decrease in the female to male ratio due to development of obstructive uropathy from the prostatic enlargement. The results of this study are in line with the general observation regarding the age groups (Stansfeld J.M 1966) (9). In the present study, non-fermenter GNBs were found to be significant in 09.44% cases, second only to the fermenters (81.27%). Pseudomonas aeruginosa is an established pathogen of urinary tract. (Rambaugh K.P et al 1999) (10). Pseudomonas spp. was the commonest non-fermenter isolate in the present study being significant in 07.63% of cases. Acinetobacters are ubiquitous in environment and in hospitals (Quinn P.J
Pseudomonas aeruginosa is.

followed by Ciprofloxacin and Ceftazidime in

, 85 were

were sensitive to at least one of the first and second line antibiotics invitro, 15 were from inpatients. This could be due to the fact that most of these isolates may be from UTI with nosocomial origin (Marcus N et al) (16).

Non-fermenters were found to be significant in 120 cases, in which 76 were in-patients and 44 were attending Outpatients Department. In this, 61 were males and 59 females. Children below 15 years of age were ten in which six were males and four females. In the remaining 110 cases, 62 were in the age group between 15 to 50 years (20 males & 42 females) and 48 were above the age of 50 years (37 males & 11 females).

Out of 97 isolates of Pseudomonas spp., 85 were sensitive to at least one of the first and second line antibiotics. Further, 69 (71.13%) isolates were sensitive to Aminoglycosides, but Gentamicin was effective against only 36 (37.11%) isolates. 42 (43.30%) isolates were sensitive to Ciprofloxacin (fluoroquinolone) whereas 73 (75.25%) isolates were sensitive to Piperaclillin (Anti-Pseudomonas Penicillin) and 31 (31.95%) isolates were sensitive to Ceftazidime (Anti-Pseudomonas Cephalosporin). 12 isolates were tried with the susceptibility of Imipenem, Piperaclillin- Tazobactam, Cefoperazone-Sulbactam, Aztreonam, Cefpirome and Ticarcillin-Clavulanic acid. 11 (91.66%) were sensitive to Imipenem, 5 (41.66%) were sensitive to Piperaclillin-Tazobactam and 6 (50%) were sensitive to Cefoperazone-Sulbactam. All 12 (100%) isolates were resistant to Aztreonam, Cefpirome and Ticarcillin-Clavulanic acid. Illustration 3 and 4.

Out of 23 isolates of Acinetobacter spp., 17 (73.91%) were sensitive to at least one of the first and second line antibiotics. Further, 17 (73.91%) isolates were sensitive to Aminoglycosides, but Gentamyacin was effective against only 10 (43.47%) isolates. None of the isolates (0%) were sensitive to Penicillins and Cephalosporins. Fluoroquinolone (Norfloxacin) sensitivity was seen with 8 (34.78%) isolates. Third line antibiotic sensitivity was performed for 6 isolates. All six (100%) were sensitive to Imipenem and Four (66.66%) isolates were sensitive to Cefoperazone-Sulbactam where as Piperaclillin-Tazobactam was effective against 3 (50%) isolates and Cefpirome sensitivity was seen with only 2 (33.33%) isolates. None of the isolates in this category were sensitive to Aztreonam and Ticarcillin-Clavulanic acid. Illustration 5 and 6.

Urinary tract infections are found in all age groups. The incidence is higher in male infants due to presence of congenital anomalies (Stansfeld J.M 1966) (8). From adulthood to the age group of 65 years, the incidence of UTI is very high in women as compared to men. In older patients there is a progressive decrease in the female to male ratio due to development of obstructive uropathy from the prostatic enlargement. The results of this study are in line with the general observation regarding the age groups (Stansfeld J.M 1966) (8). In the present study, non-fermenter GNBs were found to be significant in 09.44% cases, second only to the fermenters (81.27%). Pseudomonas aeruginosa is an established pathogen of urinary tract. (Rambaugh K.P et al 1999) (15). Pseudomonas spp. was the commonest non-fermenter isolate in the present study being significant in 07.63% of cases. Acinetobacters are ubiquitous in environment and in hospitals (Quinn P.J 1988) (6). They account for 1 to 3 percent of nosocomial infections, being second only to P. aeruginosa as non-fermenters in their recovery from clinical specimens. (Hall G.S 1995) (5) Acinetobacters have been implicated in causation of a variety of illness including UTI. (Pederson M.B et al 1970) (5) They accounted for 01.80% cases in this study. A high level of drug resistance was observed in general for majority of strains of these bacterial species in different studies (Gupta V et al 2002) (10) (Neneke A et al 2008) (11) (Jombo G.T.A et al 2008) (16) (Takeyama K et al 2008) (15) which is in line with the results of this study. Out of the 18 non-fermenter urinary isolates which were resistant to all first and second line antibiotics invitro, 15 were from inpatients. This could be due to the fact that most of these isolates may be from UTI with nosocomial origin (Marcus N et al) (16).
in the group of third line reserved antibiotics. For Acinetobacter spp., Aminoglycosides in the group of first and second line antibiotics and Imipenem in the group of third line reserved antibiotics are found to be most effective.

A previous study has reported that for *Pseudomonas aeruginosa*, amikacin, ceftazidime and piperacillin are the recommended antibiotics (Gupta V et al 2002) which is in accordance with the results of our study. But other studies reported multiple drug resistance in *Pseudomonas aeruginosa* isolates (Takeyama K et al 2008) (15), (Jombo G.T.A et al 2008) (14), (Katsumi Shigemura 2006) (13). It has been also reported that *Acinetobacter* infection in hospitalised patients showed high degree of resistance to almost all the antibiotics used routinely necessitating its susceptibility testing for newer drugs (Gupta V et al 2002) (15) which is supported by our study. Also, all strains of Acinetobacter spp. were found sensitive to imipenem in our study though emergence of resistance to this group of antibiotics has been reported in previous studies (Jamal W et al 2009) (11) (Nenek A et al 2008) (12).

From the present study it can be concluded that non-fermenter gram negative bacilli though regarded as contaminants are important bacteria causing hospital and community acquired UTI. If recovered in pure culture, a repeat urine specimen should be taken to confirm their presence, and the strain should be identified up to the species level along with the antibiotic susceptibility testing for routinely used antibiotics.

References:

15. K. Takeyama et al, Multidrug-resistant Pseudomonas aeruginosa isolated from the urine of patients with urinary tract infection, J of Infection and Chemotherapy 2008, 8(1); 59-63.
Reviews

Review 1

**Review Title:** prevalence of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospitals

Posted by Dr. Sugandi Rao on 07 Feb 2011 09:18:02 AM GMT

| 1 | Is the subject of the article within the scope of the subject category? | Yes |
| 2 | Are the interpretations / conclusions sound and justified by the data? | Partly |
| 3 | Is this a new and original contribution? | No |
| 4 | Does this paper exemplify an awareness of other research on the topic? | No |
| 5 | Are structure and length satisfactory? | Yes |
| 6 | Can you suggest brief additions or amendments or an introductory statement that will increase the value of this paper for an international audience? | No |
| 7 | Can you suggest any reductions in the paper, or deletions of parts? | No |
| 8 | Is the quality of the diction satisfactory? | No |
| 9 | Are the illustrations and tables necessary and acceptable? | No |
| 10 | Are the references adequate and are they all necessary? | Yes |
| 11 | Are the keywords and abstract or summary informative? | Yes |

**Rating:** 3

**Comment:**
This article does not add anything new. It is well known that P. aeruginosa is an important cause of nosocomial UTI.

Paper is not well written, there are typographical errors, e.g., even 105 which is significant count is written like this. Could not see the illustrations, hence results are few sentences.

Patient details regarding UTI due to Non-fermenters should have been included, hence it is not clear patients are from community or hospitalised. It has written as inpatients and OPD patients this does not explain much.

Predisposing factors for inpatients should have been discussed.

In Conclusion first sentence is nonfermenters are regarded as contaminants, but authors didn’t make any attempt to rule out contamination, since these organisms are common hospital flora, they can grow well in urine, repeat isolation was necessary.

In discussion results are not discussed and correlated.

**Competing interests:** No

**Invited by the author to make a review on this article?** : No

**Experience and credentials in the specific area of science:**
Clinical Microbiologist for 25 years.

**Publications in the same or a related area of science:** No

**How to cite:** Rao S. prevalence of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospitals [Review of the article ‘Prevalence Of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospital’ by]. WebmedCentral 2011;2(2):WMCRW00444
Review 2

Review Title: urinary tract infections

Posted by Dr. Birgit Pruess on 11 Jan 2011 02:57:42 PM GMT

1. Is the subject of the article within the scope of the subject category? Yes
2. Are the interpretations / conclusions sound and justified by the data? No
3. Is this a new and original contribution? Yes
4. Does this paper exemplify an awareness of other research on the topic? Yes
5. Are structure and length satisfactory? No
6. Can you suggest brief additions or amendments or an introductory statement that will increase the value of this paper for an international audience? No
7. Can you suggest any reductions in the paper, or deletions of parts? No
8. Is the quality of the diction satisfactory? No
9. Are the illustrations and tables necessary and acceptable? No
10. Are the references adequate and are they all necessary? Yes
11. Are the keywords and abstract or summary informative? Yes

Rating: 3

Comment:
I could not see any figures or tables to demonstrate the data. The entire results section is only a few lines with some percentage numbers. And it is not clear what the reference is for the percentage.

The topic is relevant, but the paper needs more data before it becomes relevant. The Discussion is more of a literature review. It is supposed to put the own data into perspective with the literature, but that would require more data than currently presented.

The language needs improvement.

Competing interests: no

Invited by the author to make a review on this article? : No

Experience and credentials in the specific area of science:
20 years in microbiology

Publications in the same or a related area of science: No

How to cite: Pruess B.urinary tract infections[Review of the article 'Prevalence Of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospital ' by ].WebmedCentral 2011;2(1):WMCRW00359
Review 3

Review Title: patogenicity of NFGNB in causing is unanswered

Posted by Dr. Madhusudhan Ns on 11 Jan 2011 09:38:18 AM GMT

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Rating: 5

Comment:
The pathogenic role of isolates in causing UTI is unanswered. Repeated isolation of the same organism from the same sample is not mentioned in materials and methods but concluded that pathogenic role of NFGNB in UTI to be confirmed by repeated isolation.

can Acinetobacter cause community acquired UTI? duration of patients hospital stay is not mentioned .. hence all the cases are community acquired..?

patient response to therapy is not followed , thereby given that repeated isolation not done, some of them are OPD cases, pathogenicity of acinetobacter causing UTI in OPD patients unexplained .... can these isolates considered to be pathogens..

Invited by the author to make a review on this article? : No

Experience and credentials in the specific area of science:
has been performing antibiotic sensitivity tests on clinical isolates since five years

Publications in the same or a related area of science: No

How to cite: Ns M, patogenicity of NFGNB in causing is unanswered[Review of the article 'Prevalence Of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospital ' by ], WebmedCentral 2011;2(1):WMCRW00358
Review 4

Review Title: Prevalence Of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospital

Posted by Dr. L. Caetano M Antunes on 11 Jan 2011 01:24:19 AM GMT

1. Is the subject of the article within the scope of the subject category? Yes
2. Are the interpretations / conclusions sound and justified by the data? Yes
3. Is this a new and original contribution? Yes
4. Does this paper exemplify an awareness of other research on the topic? Yes
5. Are structure and length satisfactory? Yes
6. Can you suggest brief additions or amendments or an introductory statement that will increase the value of this paper for an international audience? No
7. Can you suggest any reductions in the paper, or deletions of parts? No
8. Is the quality of the diction satisfactory? No
9. Are the illustrations and tables necessary and acceptable? No
10. Are the references adequate and are they all necessary? Yes
11. Are the keywords and abstract or summary informative? Yes

Rating: 4

Comment:
The manuscript by Shobha et al. describes a survey of the prevalence of non-fermenters in urinary tract infections as well as their antimicrobial susceptibility profiles. Although studies of this nature are important for the monitoring of the microbial pathogens causing UTIs as well as the development of antibiotic resistance, there are several issues with the paper that should be resolved in order to increase quality.

First, the paper could benefit from a more careful language revision. There are lots of typos and even a repetition of two paragraphs in the Discussion and Conclusion section.

Whenever the authors refer to percentages, they should state more clearly if they are referring to the % of the total number of strains or % of the number of strains in a certain group (non-fermenters, for example).

Lastly, in the manuscript there are references to illustrations that can not be found in the PDF file or the website.

Competing interests: No.

Invited by the author to make a review on this article? : No

Experience and credentials in the specific area of science:
I am a microbiologist with 14+ years of experience.

Publications in the same or a related area of science: No

How to cite: Antunes L. Prevalence Of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospital [Review of the article "Prevalence Of Non-fermenters In Urinary Tract Infections In A Tertiary Care Hospital" by ]. WebmedCentral 2011;2(1):WMCRW00356
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