

CORRELATION OF CLINICAL TO BACTERIOLOGICAL FINDINGS OF THE UPPER AND LOWER RESPIRATORY TRACTS IN LONG TERM CARE PATIENTS

By

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ABSTRACT

LTC patients are liable to various infections due to altered immune and anatomical barriers. We aimed to identify the correlation of bacteriological and clinical findings of the URT represented by nasal and oropharyngeal swabs, in addition to clinical examination, and their impact on LRT infection. We found that LTC patients are prone to abnormal pathogens in a unique pattern, and that LRT infection is associated with very high incidence of swabs positive for uncommon pathogens from the URT.

INTRODUCTION

Over several years, several researchers have been interested in the

mode and rate of infection of the lower respiratory tract in long term care (LTC) facilities, specially those on mechanical ventilation and/or with tracheotomy, but there have been a few, if any, that have been interested in the upper respiratory tract, namely the nose and the pharynx.

The normal flora of the nose and pharynx is well known, and when infection settles in, it is usually due to colonization by pathological organisms. In case of LTC patients, although these facts are mostly true, other factors contribute to the abnormal colonization and/or subsequent infection of the nose and pharynx. Of these factors, is "immune exhaustion"

or the potentially disabling effects of depleted, dysfunctional, or inhibited immune resources that may impair defense against pathogens¹. In addition, chronic co-morbidities with high prevalence in LTC patients may render them susceptible to infection by impairing innate or adaptive responses². For example, LTC patients frequently are elderly, and several phenomena associated with a variety of components of an aging immune system may impair pathogen defense³⁻⁶ so-called "immune senescence", a term encompassing a variety of observations in animals and humans, such as impaired vaccine responsiveness⁷. Diabetes, chronic renal insufficiency, and pre-existing cardiopulmonary disease such as chronic obstructive pulmonary disease (COPD) are frequent co-morbidities. In COPD, airway alterations may compromise local defenses, and such patients may have impaired humoral and cellular immune responses⁸. Abnormal leukocyte function described in insulin-requiring and noninsulin-requiring diabetes mellitus may in part explain the higher incidence of infection and increased morbidity seen in this disease^{9,10}. It is widely accepted that patients with renal failure have an increased risk of

infection. Laboratory studies have established defects in cellular immunity, neutrophil function, and complement activation^{11, 12}, and aluminum toxicity may contribute to immunologic impairment in chronic renal failure¹³.

Additionally, over a prolonged LTC facility stay, numerous debilities may accumulate and further contributes to infection susceptibility. Particularly important among these are nutritional deficiency^{14,15} micronutrient deficiency^{16,17} protein depletion in general¹⁸ and intensive use of corticosteroids¹⁹. Nearly universal at the inception of LTC are metabolic derangements include bone hyperresorption and male hypo-testosteronism, frequently with vitamin D deficiency^{20,21}. Vitamin D may affect cellular immune functions including maturation and monokine production by macrophage-like cells^{22,23}.

Adding to these, the experience of pain and its treatment with opioid analgesia^{24,26} anxiety^{27,28} and depression^{29,30} that accompany critical illness may induce an array of immune alterations.

In the upper airway additional factors may contribute, the presence of

tracheostomy with breaching of natural barriers, or nasogastric tubes for feeding with subsequent pressure necrosis, stasis, or simply acting as foreign body all invite abnormal organism colonization and subsequent infection.

Nasal commensals in the normal population include *Streptococcus viridans*, *Streptococcus pneumoniae*, *Staphylococcus* species, *Micrococci*, *Diphtheroids*, and *Hemophilus* species, while possible pathogens include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Corynebacterium diphtheriae*, *H. influenza*, and *Klebsiella* species³¹.

Organisms that are considered to be normal commensals of the oropharynx in the normal population are *Streptococcus viridans*, non-hemolytic *Streptococci*, *Streptococcus pneumoniae*, *Staph epidermis*, *Diphtheroids*, *Branhamella catarrhalis*, *Bacteroids*, and *H. influenza*, while possible pathogens include *Streptococcus pyogenes*, *Corynebacterium diphtheriae*, and Vincent's organisms³¹.

As any part of the body, the nose and pharynx are susceptible to infec-

tions. Neglecting these two areas as a source of sepsis or contamination to the lower respiratory tract (LRT) has long been true.

AIM OF THE STUDY

In our study, we aimed at identifying the incidence of contamination of the nose and oropharynx of LTC patients with pathogenic organisms, the clinical correlation of signs and symptoms to the laboratory findings, and finding any relation to LRT infections.

MATERIAL AND METHODS

A prospective study was designed. The study was to include all the long-term care patients admitted in two secondary referral medical centers during the study period, which was designed to be one year, from September 2002 to August 2003. No informed consent was mandatory, because the observational study did not modify current diagnostic or therapeutic strategies.

Exclusion criteria were any patient with prior immune deficiency diseases (except for diabetes), failing to survive for at least 6 months in the facility, or any neoplasm in the area of upper or lower airway.

As routine, admitted patients in addition to routine clinical screening examination, were subjected to oropharyngeal and nasal swabs that underwent aerobic and anaerobic cultures. Swabs were retaken on monthly basis, except if any apparent additional event surfaced requiring an additional culture. Routinely, clinical examination of the patients on weekly basis was carried out, and if the patient was conscious, nasal, oropharyngeal, or chest symptoms were inquired for on daily basis. All findings were documented in a special form designed for the study. Another indication to additional swabs and examinations was the development of LRT infection.

If at any point, the culture results were found abnormal, additional examinations were carried out, and vice versa. Also in case of proof of URT infection, the LRT was examined and vice versa.

In cases of LRT infection, either sputum, or tracheal aspirates were obtained for culture.

At the end of the period of one year all, the collected data was revised, tabulated, and statistically analyzed.

RESULTS

The study was carried out during the period of one year, it included 63 patients that were followed up for at least 6 months in two secondary referral hospitals' LTC facilities during which they were subjected to the research protocol. Of the 63 patients, 54 were over the age of 60, 7 were children (below age of 16), and 2 were adults between 16 and 60 years. There were 36 males and 27 females. Of the 63 patients, 23 were tracheostomized permanently, and only 12 were conscious.

The results of swabs and clinical examinations of the patients were tabulated as shown in tables 1 and 2.

A total of 883 nasal swabs and 929 pharyngeal swabs were taken from the patients during the study period. Of the nasal swabs, 192 proved positive for abnormal flora, while of the pharyngeal swabs, 331 proved positive for abnormal flora.

The 4 most commonly encountered pathogens were *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Klebsiella*, and *Methicillin resistant staphylococcus aureus* (MRSA).

Pt N°	Age & Sex	Diagnosis	Add	Months of study
1	63 M	CVS-D-H-RF	T	12
2	67 M	CVS-H		12
3	72 F	CVS-D-H	T	12
4	87 M	CVS-D-H	T	12
5	66 M	CVS-D-H-RF	T	12
6	70 M	CVS-D		11
7	73 M	CVS-D-H		12
8	24 M	MTA-BL	T	12
9	66 F	CVS-H	C	10
10	62 M	CVS-D-H		12
11	76 F	ALZ-H-D	C	9
12	72 F	CVS-H-RF		8
13	14 F	CP-MR		12
14	69 F	CVS-D-H		12
15	83 M	CVS-H		9
16	21 M	MTA-BL	T	12
17	60 M	CVS-D		12
18	64 M	CVS-H		12
19	8 F	CP-MR	T	12
20	67 M	CVS-D-H-RF	T	12
21	76 F	CVS-H		8
22	72 M	CVS-D-H		12
23	7 M	CP-MR	T	12
24	80 F	ALZ-D-H	T	7
25	61 M	CVS-D	C	12
26	67 M	CVS-D-H		12
27	11 F	MCA-BL	T	12
28	77 M	CVS-H		12
29	67 F	CVS-D	C	11
30	65 M	CVS-D-H-RF	T	11
31	69 M	CVS-D-H		11
32	12 M	CP	T	11
33	60 M	CVS-D	C	11
34	65 M	CVS-D-H-RF	T	11
35	60 M	CVS-D-H		11
36	69 F	CVS-D-H	C	11
37	72 F	ALZ-H		10
38	10 F	CP-MR	T	10
39	75 M	CVS-D-H		10
40	67 F	CVS-H	C	10
41	62 M	CVS-D	C	10
42	77 F	ALZ-H-D-RF	T	9
43	9 M	CP		9
44	87 F	CVS-H	T	9
45	82 M	CVS-H	T	9
46	86 M	CVS-D-H	T	9
47	73 M	CVS-H		9
48	63 M	CVS-D	C	9
49	69 M	CVS-D-H		9
50	66 M	CVS	C	9
51	90 F	ALZ-D-H-RF	T	7
52	67 M	CVS-H		8
53	61 M	CVS-H	C	8
54	67 M	CVS-D-H	C	8
55	62 M	CVS-D		8
56	87 M	ALZ-D-H		8
57	69 F	CVS-D		7
58	77 F	CVS-D-H	T	7
59	71 M	CVS-D		7
60	92 F	CVS-D-H-RF	T	6
61	60 M	CVS-D-H		7
62	67 M	CVS-H		7
63	72 F	CVS-D-H	T	7

Table 1: Demographic data of patients, and their medical condition

CVS=cerebrovascular stroke, D=diabetes mellitus, RF=renal failure, H=hyperension, MTA=motor car accident, ALZ=Alzheimer's disease, MR=mental retardation, CP=cerebral palsy, BL=brain laceration, T=traumatized, C=conscious

Nasal swabs;

Total number of swabs	No of swabs with normal flora	No of swabs with pathogens
883	691 (78.3%)	192 (21.7%)

Pattern of swabs

Organism	N° of +ve swabs(%)	N° of associated clinical URT affection(%)	N° of associated clinical LRT
Strep pyogenes	103(53%)	43 (41%)	26 (25%)
Pseudomonas	43 (23%)	32 (74%)	16 (37%)
Klebsiella	33 (17%)	9 (27%)	2 (6%)
MRSA	13 (7%)	4 (30%)	4 (30%)

Pharyngeal swabs;

Total number of swabs	No of swabs with normal flora	No of swabs with pathogens
929	598 (64.4%)	331 (35.6%)

Pattern of swabs

Organism	N° of +ve swabs(%)	N° of associated clinical URT affection(%)	N° of associated clinical LRT
Strep pyogenes	156 (47%)	76 (49%)	53 (34%)
Pseudomonas	65 (20%)	45 (70%)	37 (56%)
Klebsiella	89 (27%)	32 (36%)	15 (17%)
MRSA	21 (6%)	9 (43%)	13 (61%)

LRT affection;

Total No of attacks	Correlation to +ve nasal swabs	Correlation to +ve pharyngeal swabs
157	75 (47.7%)	131 (83.4%)

Table 2: Nasal and Pharyngeal swab results, with their correlation to clinical affection of

DISCUSSION

The welfare of patients in LTC facilities involves many aspects, and is a complex, interactive, multi-departmental teamwork. The ultimate aim is to provide the patients with the longest possible lifespan, with the least possible co-morbidities or complications. This is not easy to achieve as the patient usually is debilitated by multi-system malfunction if not failure, with the subsequent immune alteration in various aspects.

The LTC patient who is compromised by barrier breaches is likely to encounter and become colonized with nosocomial pathogens, many with enhanced antibiotic resistance and virulence. Risk factors for nosocomial acquisition and carriage identified in the any critical care or LTC environment are nearly universal: these include prolonged ventilation³², central venous catheterization³³, prior antibiotic administration^{34,36} cognitive impairment³⁷, parenteral nutrition³⁸ or alimentation through gastric feeding tubes³⁹ and urinary catheterization⁴⁰. As a result, the most important source of infection in the LTC environment is the patient himself⁴¹ in that such organisms may coat body surfaces and sites of breakdown, replace oropharynx

and GI tract flora, find a niche in tracheal and feeding tube biofilm, and contaminate intravenous and catheter sites.

Cross colonization between patients also plays an important role in the general spread of nosocomial resistant organisms such as *Pseudomonas aeruginosa*. Similarly, patients are at risk for patient-to-patient transmission of microbes. This risk may be enhanced by intensive nursing requirements for patient contact and decreased staffing ratios, and increased congestion^{42,43}. Also, patient immobilization and recumbency^{44,45} as well as inattention to isolation precautions, inadequate exchange or misuse of gloves, or inadequate adherence to hand-washing protocol may contribute to organism load⁴⁶. Bedrails, door-knobs, and even physician neckties can be colonized with potential pathogens, and facilitate patient-to-patient transfer.

The issue of being in a closed health facility that involves direct or indirect contact with other patients with other diseases is another hazard. Patients are often found to have one or the other form of chest infection, pharyngitis or rhinitis. Prevention or

expectation of such infections would be of value in reducing hazards of exposure to the infection itself, and reduce the complications due to exposure to the side effects of various drugs administered.

Our study aimed to identify the most common abnormal pathogens that colonise in the upper airway through the patients' stay in the facility for a period extending at least 6 months, namely the nose and the oropharynx, the incidence of subsequent actual clinical affection of these regions by the pre-isolated pathogens, and the incidence of associated LRT affection. We also studied the incidence of URT affection in the cases that develop LRT infection through the study period, and correlating the organisms isolated from the sputum or tracheal aspirate with those isolated from the nose and the oropharynx.

Our study demonstrated that not one single patient studied passed the study period without development of an URT or LRT infection or both. The total number of patients that completed the minimum of six months study period before being deceased or transferred to another facility for one cause or the other was 63 patients. The total number of nasal swabs ob-

tained, whether as scheduled routinely, or as per indication was 883 swabs, 691 (78.3%) of which showed normal flora, and 192 (21.7%) showed abnormal or pathogenic flora.

An interesting finding was that of the most common 4 organisms isolated only two were, according to literature, potential pathogens of the URT, i.e., *Klebsiella* species and *Streptococcus pyogenes*, while the other two isolates, MRSA and *Pseudomonas* were spuriously isolated. The explanation of such finding is yet to be explained, but we propose that colonization or infection by such pathogens is due to the unique nature of LTC facilities of chronicity, relative overcrowding, immune alteration, intense and sometime overuse of antimicrobial drugs for various infections in various areas of the body.

Of the obtained swabs the degree of clinical correlation to the swab findings ranged greatly, from as low as 27% with *Klebsiella* +ve swabs, to as high as 74% with *Pseudomonas* +ve swabs. The association of a positive nasal swab with a LRT infection was within a close range for all the isolated organisms (26%-44%) except for those associated with *Klebsiella*,

where the associated LRT infection was a low 6%. Such association of nasal affection or colonization by pathogenic organisms with LRT infection is an agreement with previous studies¹ that demonstrated that such patients usually have several factors leading to the association of URT and LRT infections, including breaching of the mucosa by the feeding tubes, inhibition of normal respiratory tract secretions, that contain IgA and other antimicrobial agents along with altered mucocilliary function all along the respiratory tract.

Regarding the oropharyngeal swabs, the total swabs taken were 929 swabs, 598 (64.4%) of which were normal, and 331 (35.6%) of which contained pathogenic organisms. Of these swabs the degree of clinical correlation to the swab findings ranged from 36% with *Klebsiella* +ve swabs, to 70% with *Pseudomonas* +ve swabs. The association of a positive oropharyngeal swab with a LRT infection was within a close range for all the isolated organisms (21%-38%) except for those associated with *Klebsiella*, where the associated LRT infection was a low 12%.

So in both nasal and oropharyn-

geal swab-positive cases, there was a high clinical correlation between the bacteriological swab findings and the clinical findings in case of infection by strept. pyogenes, pseudomonas and MRSA, but a poor correlation to *Klebsiella*.

When we compared the positive swabs with associated cases of LRT infection, there was a 25% association of positive nasal swabs with LRT infection, and a 35% association with positive oropharyngeal swabs. These results reflect a higher incidence of association of LRT affection with the oropharyngeal organisms than nasal organisms despite the relatively high association with both.

On the other hand, when we correlated the LRT infection to associated positive nasal or oropharyngeal swabs, there was a 83% correlation to the oropharyngeal positive swabs, and a 47% correlation to the nasal positive swabs, signifying that there is a higher degree of association of LRT infection if there was an URT affection in the area of the oropharynx more than if the nasal area was affected. These findings agree and support the theory that in the critically ill and patients with impaired consciousness,

there is a degree of aspiration, this aspirated material carries the organisms from the oropharynx down the larynx and trachea, with subsequent LRT infection, thus the affecting organisms and the same, with high association with oropharyngeal swab correlation 47. The overall findings of the study demonstrate that there is a high incidence of colonization of the URT with pathogenic organisms in patients settled in LTC facilities, the most common are *Strep pyogenes*, *Pseudomonas*, MRSA, and *Klebsiella*. Nasal and/or oropharyngeal positive swabs are associated with high incidence of LRT infection (although higher in oropharyngeal than nasal), and very high incidences of LRT infections are associated with URT colonisation by pathogenic organisms.

Conclusion

Patients in LTC facilities are liable to infection by uncommon pathogens of the URT, specially MRSA and *Pseudomonas*. Upper respiratory tract regular swabs can predict impending or early determine LRT infection, thus guiding to early treatment, and less complications, association with clinically correlating signs or symptoms may indicate a necessity for initiation

of treatment to avoid complications or development of severer forms of infection or more resistant strains of pathogens.

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ارتباط الموجودات السريرية و البكتيرية في الجهاز التنفسي العلوي والسفلي في مرضي الرعاية طويلة الأمد

إن مرضي الرعاية طويلة الأمد عرضة لمختلف أنواع العدوى نتيجة اختلال الدفاعات المناعية والتشريحية الطبيعية. وهدف البحث إلى معرفة ارتباط الموجودات السريرية والبكتريولوجية في الجهاز التنفسي العلوي في صورة مسحات من الأنف والحلق وتأثيرها علي الجهاز التنفسي السفلي. ووجد أن مرضي الرعاية طويلة الأمد عرضة بصورة خاصة من التهابات الجهاز التنفسي. وأن معظم التهابات الجهاز التنفسي السفلي مصحوبة بنسبة عالية من المسحات الإيجابية من الجهاز التنفسي العلوي.

