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Original Article

The prevalence of rectal carriage of *Klebsiella pneumoniae* amongst diabetic patients and their clinical relevance in Taiwan: A five-year prospective study

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Abstract *Background/purpose:* Pyogenic liver abscess (PLA) and bacteremia caused by *Klebsiella pneumoniae* is a common complication among patients with diabetes mellitus (DM). The aim of this study is to investigate the prevalence of rectal carriage and serotype distribution of *K. pneumoniae* amongst DM patients and their clinical relevance.
Methods: We prospectively collected rectal swabs for *K. pneumoniae* culture in asymptomatic DM patients from March 2008 to June 2009. Seven capsular serotypes that were commonly associated with PLA were determined by capsular polysaccharide synthesis (cps) genotyping. Microbiologically confirmed bacterial infections were evaluated 1 and 5 years after initial enrolment of the patients.
Results: A total of 100 male and 62 female patients (mean age, 56.6 years) were enrolled. Of these, 77 (47.5%) had rectal *K. pneumoniae* colonization. Colonizers were older than non-colonizers ($p = 0.03$). Sex, fasting blood glucose, and initial HbA1C were not statistically different ($p = 0.26$, 0.18, and 0.31, respectively). Among the 65 available isolates, 22 (33.8%) belonged to the seven main serotypes. During the 5-year's follow-up, 21 patients developed microbiologically documented bacterial infections but none of them developed PLA and bacteremia. Risk factors for bacterial infection within 5 years included initial glycosylated hemoglobin (HbA1C) > 10% or first-year average HbA1C > 10%.

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Conclusion: Although nearly half of asymptomatic DM patients had rectal carriage of *K. pneumoniae* and one-third of them colonized by isolates belonging to the seven serotypes related to PLA, none of them subsequently developed PLA and colonized patients did not have higher risk of microbiologically confirmed bacterial infections.

Introduction

Klebsiella pneumoniae is a major nosocomial pathogen that may contribute to the development of multidrug resistance in Western countries.[1,2] However, in Taiwan it can cause severe community infections, especially pyogenic liver abscess (PLA) with serious sequelae.[3] After decades of investigations, we now know that the molecular epidemiology of *K. pneumoniae* in Taiwan is quite different from that in other countries. Serotype K1/multilocus sequence typing (ST) 23 is a major clone that causes community-onset liver abscess and other invasive infections.[4,5] The role of serotype K2 is disputed, and the STs of K2 are more diverse than K1.[6] Different serotypes of *K. pneumoniae* are associated with different clinical presentations.[6]

The bowels have been considered to be the primary reservoir of *K. pneumoniae* in hospitalized patients,[7] and antibiotic usage may increase fecal carriage of *K. pneumoniae* in hospitalized patients.[8] The colonization of *K. pneumoniae* may persist in spinal cord injury patients for a mean of 20 days.[9] Recent studies have shown that rectal carriage of *K. pneumoniae* may be the source of *K. pneumoniae* bacteremia.[10,11] Furthermore, according to a retrospective Taiwanese database analysis, ampicillin and amoxicillin use are reported to increase the risk of *K. pneumoniae* liver abscess.[12] A surveillance study about rectal carriage of healthy Chinese residents in several Asian countries showed a spectrum of carriage rates, ranging from 18.8% in Japan to 87.7% in Malaysia. Serotypes K1 and K2 accounted for 9.8% of all isolates.[13]

Diabetes mellitus (DM) has been identified as a risk factor for bacterial infection.[14,15] Previous studies have identified DM as one of the most important risk factors for *K. pneumoniae*—related PLA,[3–5] and metastatic infection was associated with poor glycemic control.[16] In addition, poor glycemic control stimulates capsule biosynthesis of highly virulent *K. pneumoniae* and contributes to bacterial invasiveness.[17] Moreover, a recent study in patients with diabetes-related foot infections showed that gut colonization with *K. pneumoniae* with carbapenemase is a risk factor for mortality.[18] It is hypothesized that carriage of virulent *K. pneumoniae* strains precedes to development of *K. pneumoniae*—related PLA,[7–12] but a prospective study is lacking. In order to understand the prevalence of rectal carriage of *K. pneumoniae* amongst DM patients and the distribution of serotypes and their clinical relevance, we performed rectal swabbing in asymptomatic DM patients and evaluated microbiologically confirmed bacterial infections at 1 year and 5 years after the patient's initial enrolment.

Methods

Hospital setting, study design, and patient enrolment

Far Eastern Memorial Hospital, an 1100-bed tertiary referral center, provides medical services for about 1 million people in New Taipei City, Taiwan. The study population consisted of adult patients >18 years old with diabetes followed up at a metabolism clinic. A study physician interviewed patients at enrolment using a standardized case record form to obtain basic information and medication history. After the intake interview, patients were eligible for enrolment if they had not used antibiotics within the previous 3 months. Patients also reviewed and signed informed consent forms. No intervention or patient interview was performed after the enrolment. A retrospective collection of bacterial infection episodes among these cases was carried out in 2016. This study was approved by the Institutional Review Board of the Far Eastern Memorial Hospital (096054, 105079-E).

Rectal swab surveillance culture

Trained nurses or the study physician used a conventional culture swab (BBL CultureSwab EZ, Becton Dickinson, Sparks, MD, USA) to obtain rectal swab samples. The rectal swab was performed by inserting the swab tube 1 cm above the anal verge. The specimen was inoculated on an eosin-methylene blue agar plate immediately. Mucoid-like colonies were selected for further identification. The identification of *K. pneumoniae* was carried out by the conventional biochemical methods. Rectal swabs were performed at enrolment.

Clinical information and subsequent bacterial infection

Clinical information was collected from the medical record. Glycosylated hemoglobin (HbA1C) was determined using a Tosoh G7 HPLC analyzer (Tosoh Bioscience, South San Francisco, CA, USA). Patients' initial HbA1C and average HbA1C during the first year after enrolment in the study were used to represent their degree of glycemic control. The diagnosis of a documented bacterial infection was based on clinical, bacteriological, and radiological criteria and was reviewed by two infectious-disease physicians 1 year and 5 years after the initial enrolment. Only

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