Prevalent nosocomial clusters among causative agents for candidemia in Hamilton, Canada

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In Canada, the incidence of candidemia, the bloodstream infection caused by *Candida* species, varied from 1.2–5.1 cases/100,000, representing the third most common type of bloodstream infections in intensive care unit patients. However, the relative contributions of nosocomial transmission in candidemia remain poorly understood. In this study, we investigated the prevalence of nosocomial clusters among the causative agents for candidemia in Hamilton, Ontario, Canada, during a period from January 2005 to February 2009. We genotyped 134 isolates from 125 unrelated patients with candidemia, among which were 87 *C. albicans*, 20 *C. parapsilosis*, 11 *C. glabrata*, 15 *C. tropicalis*, and one *C. krusei*. Our PCR fingerprinting analyses using three highly polymorphic primers identified a total of 99 genotypes, with 18 of them shared by 44 independent isolates. Nine pairs of isolates were obtained from the same patients at the same time and each pair had identical fingerprints. Interestingly, all 44 independent strains belonging to each of the shared genotypes were isolated from patients within 3-months stay in the Hamilton hospitals. Both inter- and intra-ward clusters were found, including one that contained strains from intensive care units in two hospitals. Our results indicated that 33% of the patients with candidemia were infected by nosocomial clusters and suggested that measures should be taken in hospitals to prevent nosocomial acquisition of *Candida* infections.

Keywords candidemia, PCR fingerprinting, nosocomial clusters, strain replacement

Introduction

The fungal genus *Candida* includes over 200 species which are ubiquitous in nature and are commonly found on inanimate objects, foods, plants, and animals. Many *Candida* species are normal commensals of humans, frequently inhabiting the oral mucosal surface, the gastrointestinal tract, the urogenital tract, and the skin [1–3]. However, many of these organisms are capable of causing infections, primarily in patients with compromised immunity [2,3]. Indeed, it has been known for a long time that *Candida* infection, or candidiasis, is very common among debilitated patients [4–7]. Candidiasis is broadly classified into mucocutaneous and invasive forms, with candidemia, the focus of this study, belonging to the latter group in that it involves the presence of *Candida* species in blood. The common risk factors for invasive candidiasis include HIV infection, immunosuppressive therapy, recent surgery, presence of central line, prolonged stay in the intensive care unit (ICU), and for small children, a very low birth weight [1–7]. Over the past 10 years, the incidence of candidemia in hospital ICUs has increased significantly in some regions of the world, and nosocomial infections have been hypothesized as a major contributor [1–3].

Strains causing nosocomial infections could be from two sources, i.e., from endogenous strains brought into the hospital by patients themselves or nosocomial transmission from the hospital environment. Several studies have implicated nosocomial transmission from a common source including contaminated infusates, the hands of health-care workers, hospital food, and medical devices [4,6,8–11]. If the isolates were from an endogenous source and patients were unrelated, they should be genetically different from each other without any spatial and temporal clustering. In contrast, if the strains were from a common source from within the hospital environment, clusters of isolates with

similar or identical genotypes should be found and these strains should show spatial and temporal clustering.

With the development of modern molecular techniques for genotyping, it is now possible to examine the relationships among strains and to identify whether they are from the same or difference sources [12,13]. Indeed, with the aid of discriminatory molecular markers, genotyping has enabled investigators to identify and cluster strains, as well as to set apart these clustered strains from one another based on temporal and geographical factors [14–18]. In this study, a nosocomial cluster is defined as the isolation of strains sharing identical genotypes at the examined markers and that the strains were obtained from ≥ 2 patients in the same hospital within a period of 90 days [1].

A previous retrospective study conducted by Yamamura *et al*. [19] demonstrated that between 1992 and 1994, 88.4% of the patients with candidemia across Canada were adults. They found that the majority of the clinical isolates (69%) belonged to one species *C. albicans* and patients > 60 years old who were in ICUs were at the highest risk. However, no genotypic information was available for that latter group of isolates. In a recent epidemiological study performed in Iceland, Ásmundsdóttir *et al*. [4] demonstrated that 33% of candidemia could be attributed to nosocomial clusters. Their conclusion was based on DNA fingerprinting by PCR using arbitrary primers, which has been observed to have a high discriminatory power for related and unrelated isolates of clinically relevant *Candida* species [14–18]. Ásmundsdóttir *et al*. [4] concluded that the risk of candidemia in hospitals varied among wards, with the highest being in ICUs. Since the last retrospective study in the early 1990s there is little information on the relative roles of nosocomial clusters in causing candidemia in Canada, we sought to investigate the prevalence of nosocomial clusters in Hamilton, Ontario, Canada.

This study investigated whether nosocomial clusters of strains causing candidemia were present in three tertiary care hospitals, part of Hamilton Health Sciences (HHS), in Hamilton, Ontario, Canada, and if so, their prevalence within and among wards, as well as within and among hospitals. We were also interested in the potential changes in the distribution of *Candida* species causing candidemia over the 10 years since the last epidemiological survey was conducted in the 1990s in this region [19]. Several recent studies [1–5] have shown a growing incidence of non-*C. albicans Candida* species causing candidemia. Whether a similar shift occurred in this region is unknown. Information from this study should help identify the importance of nosocomial transmission and help develop strategies to prevent the increasing incidence of nosocomial candidemia.

Materials and methods

Strains

Candida isolates were obtained from patients with candidemia who had been admitted to HHS hospitals from 1 January 2005 to 28 February 2009. Blood cultures were incubated using the BacTAlert system (bioMérieux Canada Inc, St. Laurent, Quebec). Isolates were identified to the species level with the use of standard morphological and physiological tests available in clinical microbiology labs, i.e., germ tube formation, a set of macroscopic and microscopic features on bile oxgall agar, and physiological characteristics determined through the use of the Vitek Legacy YBC (bioMérieux; 2005–2007), Vitek 2 YST card (bioMérieux; 2007–present), and API 20C AUX (bio-Mérieux) as required.

The clinical history for each of these patients was retrieved retrospectively by two of the investigators (HM and DY) using a standardized form. The patient's age, sex, the ward location within the admitted hospital, underlying diseases, treatment regimens for invasive candidiasis, dates of the first *Candida*-positive blood culture, as well as subsequent dates with positive blood cultures were collected. Following traditional guidelines, an episode of candidemia was defined as ≥ 1 blood culture positive for *Candida* species and episodes that happened 30 d apart or were caused by different species of *Candida*, were considered as separate cases of candidemia [4].

DNA extraction and genotyping

Isolates were stored at $-80°C$ at the Microbiology Laboratory of Hamilton General Hospital. In total, 161 isolates of *Candida* spp. were recovered from blood cultures during the study period, of which 152 were stored but only 134 proved to be viable and used for subsequent genotypic analyses. To obtain DNA for genotyping through PCR fingerprinting, all isolates were first streaked onto yeast extract-peptone-dextrose agar (Fisher Scientific, Fair Lawn, NJ, USA) and incubated 48 h at 33°C. Genomic DNA was extracted from the actively growing yeast cells using protoplasting buffer and lysing buffer, followed by isopropanol precipitation as described in Xu *et al*. [18]. The extracted DNA was stored at $-20°C$ and diluted to working concentration (~ 50–100 ng/ml) before being amplified by PCR using the following three separate primers: $(GACA)_4$ (5′-GACAGACA-GACAGACA-3′), OPA3 (5′-AGTCAGCCAC-3′), or M13 (5′-GTAAAACGACGGCCAGT-3′) [4–6]. Each standard PCR contained 8 μl of Ready-to-Go-PCR mix (Promega, Madison, WI, USA), 4 μl of working concentration of template DNA, and 4 μl of 0.10 μM of the desired primer. The amplified products were subjected to gel electrophoresis on 1% agarose gels with $1 \times$ Tris-Borate-EDTA buffer (pH 8)

for 3 h at 100 V. Ethidium bromide was added to the gels prior to loading the PCR products and upon completion of the electrophoresis, the gels were photographed digitally under ultraviolet light using a Chemi-Imager (Alpha InnovTech Corporation, San Leandro, CA, USA). Representative strains from each of the analyzed species were tested multiple times for PCR and gel electrophoresis to check for reproducibility of the PCR-fingerprinting patterns.

Data analysis

All the amplified DNA bands for all samples were scored and as in previous studies, a position tolerance setting of 2% was used [4,16]. Strains with identical fingerprint patterns for all analyzed primers were considered to have the same genotype and belong to the same clone. To ensure consistency and minimize scoring errors, the PCR fingerprinting patterns were scored two times, each time by two different people. These genotypes were then compared to patient history to identify nosocomial clusters which we defined as a group of isolates with an identical genotype obtained from ≥ 2 patients in the same hospital system within a period of 90 d. Our definition is more stringent than those used in previous studies, which employed 95% of PCR fingerprint identity as a cutoff for nosocomial clusters [4,16]. The phylogenetic analysis program PAUP* (Sinauer Associates, Sunderland, MA, USA) was used to construct a phenogram illustrating strain relationships and identifying clusters of strains.

Discriminatory index

Following PCR amplification and DNA band scoring, phylograms were constructed independently for the fingerprinting pattern of each primer using PAUP*. The discriminatory index (DI) for each primer for each species was calculated using the Simpson's Diversity Index, following previous studies [1,18].

Test for temporal clustering of strains

Temporal clustering of strains was assessed via two additional tests that examined the relationship between pairwise genetic distances of strains and their times of isolation. These tests were conducted for each of the four *Candida* species where multiple isolates were recovered. Here, the pairwise genetic distance between each pair of strains was calculated based on band sharing using the program PAUP* and the temporal difference between their times of isolation (i.e., number of days separating the isolation time of the two strains) was derived from the retrieved patients' records.

Using the obtained genetic distance and the temporal time difference data, the first test examined Pearson's correlation coefficient between these two variables. This analysis was conducted separately for each species. In the second test, pairs of isolates were divided into two groups, one group consisting of strain pairs that were obtained less than 90 d from each other and the other group including strains separated by greater than 90 d of each other. The mean genetic distances and standard deviations were calculated for each of the two groups for each *Candida* species. The *t*-test was conducted to determine the statistical significance of the observed difference between the two groups using the software package SPSS version 14 (SPSS Inc, Chicago, IL, USA).

Results

Based on our retrospective data, 161 isolates associated with candidemia were recorded, of which 29 were duplicates (i.e., isolated from the same body site of the same patient at the same time). Thus, there were 132 episodes of candidiasis at HHS during the study period and 132 independent, separate isolates (Table 1). Among these 132 episodes, 89 were caused by *C. albicans*, 19 by *C. parapsilosis*, 12 by *C. tropicalis*, 10 by *C. glabrata,* and two by *C. krusei* (Table 1). *Candida albicans* was the most prevalent species causing candidemia in the HHS hospital environment, accounting for 67% of the total yeast isolates (Table 1).

Among the 161 isolates, 134 isolates were successfully revived and further analyzed, of which nine were duplicates having the same PCR fingerprinting profiles. In order to minimize the effects of duplicate isolates on our analyses, only one representative strain from each of the nine was included in the calculations of discriminatory index and nosocomial clusters (Table 1). The only exception was the four sequential strains from one patient that belonged to two different genotypes (see section *Strain clusters* below).

Of the three primers used, M13 had the highest DI in identifying genotypes of *C. albicans*. However, OPA3 possessed the highest DI for identifying the genotypes of the three other species that contained multiple strains (Table 2). When DNA fingerprint results from all three primers were analyzed together, their strain genotype DIs for *C. albicans*, *C. tropicalis*, *C. parapsilosis* and *C. glabrata* were 0.92, 0.90, 0.83 and 0.83, respectively (Table 2). The average DI including all the markers was 0.87 for the four species analyzed here. Our PCR fingerprinting results were consistent with species identifications of the 125 isolates based on morphological and physiological characteristics. Clear differences in the banding patterns were observed among strains belonging to the five *Candida* species.

Table 1 Summary information for patient and yeast species demographics of the strains causing candidemia in Hamilton, Ontario, Canada from 2005–2009.

Candida species or patient age	Total number of patients with candidemia			Number of isolates genotyped in this study (Number of duplicates)
	Male patients	Female patients	Total number of isolates obtained from these patients (Number of duplicates)	
Mean age of patients	55	68	-	-
C. albicans	39	50	100 (11)	87 (1)
C. glabrata	5	5	14 (4)	11 (1)
C. parapsilosis	11	8	27 (8)	18 (4)
C. tropicalis	8	4	18 (6)	15 (3)
C. krusei	0	2	2 (0)	1 (0)
Total	63	69	161 (29)	134 (9)

Epidemiology

Of the 132 patients with candidemia, 63 were male and 69 were female. The mean age was 62 years (range six months to 87 years) with a higher age in females (68 vs. 55 years). The mean age of candidemia patients increased by 10 years compared to that from the previous survey (mean age 52 years) from this region [19]. The most prevalent risk factors for the current study population were the use of antimicrobial therapy (90%) and presence of a central line (68.2%).

Strain clusters

Among the 86 strains of C. *albicans*, a total of 69 genotypes were identified. Nine of these were each shared by two or more strains while the remaining 60 genotypes were represented by one strain each (Fig. 1). Among the nine shared genotypes, the most common was shared by five strains, two were shared by four strains each, one by three strains, and five by two strains each. Of these nine clusters, three were found in the ICU of one hospital, with two simultaneously present in the ICU of two hospitals. Strains CA05 and CA33 were found at hospital A, while CA34 and CA43 were found at hospital B (Fig. 1). *Candida albicans* clusters were observed to exist at all hospital sites. Ten different genotypes were found among the 12 independent

Table 2 The discriminatory index of the PCR fingerprint pattern using three primers M13, (GACA)$_4$ and OPA3 across the four species: *Candida albicans, C. tropicalis, C. glabrata,* and *C. parapsilosis.*

Species	PCR fingerprinting primers			Mean DI[*] per species
	M13	(GACA)$_4$	OPA3	
C. albicans	0.95	0.90	0.91	0.92
C. tropicalis	0.90	0.88	0.92	0.90
C. parapsilosis	0.83	0.80	0.87	0.83
C. glabrata	0.77	0.79	0.93	0.83
Average DI per Primer	0.86	0.84	0.91	0.87

[*]DI, Discriminatory index.

C. tropicalis strains analyzed. Two of these genotypes were shared by two strains each (Fig. 2). Both clusters of *C. tropicalis* were from the same hospital. For *C. glabrata*, seven genotypes were observed among the 10 strains, of which three were shared by two strains each (Fig. 3). All three clusters were present in one hospital, with one cluster found in the ICU ward. Twelve genotypes were identified among the 18 *C. parapsilosis* strains analyzed (Fig. 4). Of these, two were shared by two strains each and two were shared by three strains each (Fig. 4). These four clusters of *C. parapsilosis* were found in two different hospitals. It should be noted that these 18 strains in Fig. 4 were from 15 patients with four strains (CP92, CP94, CP102 and CP105) from one patient but they were isolated one week apart from each other during a 4-week span. Strains CP92 and CP94 were from the first two weeks and strains CP102 and CP105 were from the later two weeks. The differential clustering of strains CP92, CP94, CP102 and CP105 from one patient foreshadowed a single case of *C. parapsilosis* strain replacement and represented two independent episodes of candidemia (Figs. 4 and 5).
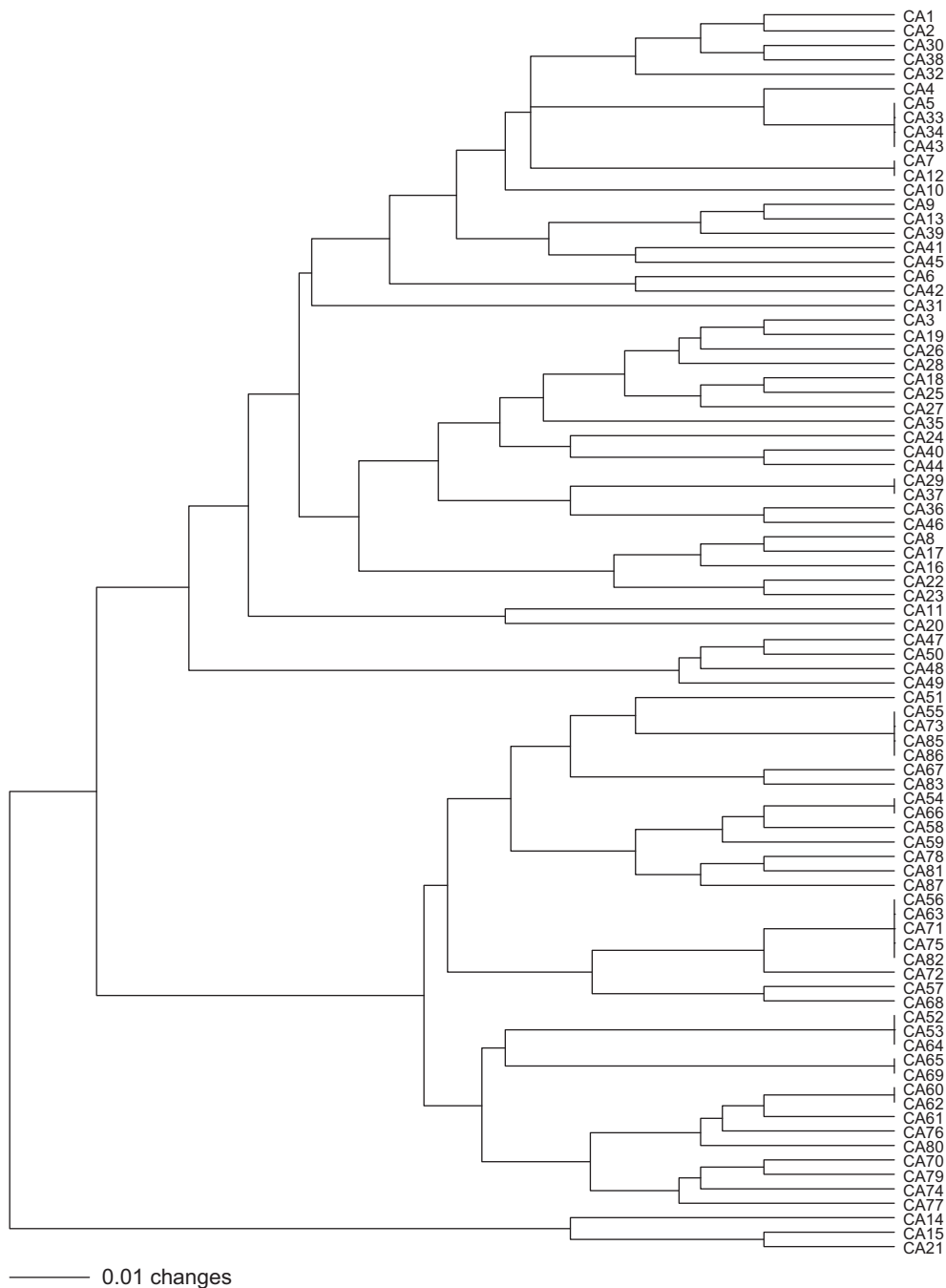
Temporal genotypic clustering of strains

The mean difference between pairs of strains in their banding patterns was 16.48% for *C. albicans*, 43.65% for *C. glabrata*, 28.14% for *C. parapsilosis* and 32.21% for *C. tropicalis* (Table 3). These results suggest abundant diversity within each of the species and that the observed intra- and inter-ward clusters within hospitals and the inter-hospital strain clusters were neither due to the lack of polymorphisms for the markers nor due to the lack of diversity in the population samples (Table 3). Furthermore, we found significant positive correlations between the pairwise genetic distance and the pairwise temporal time difference across the four-year study period for each of the four *Candida* species ($p < 0.05$; detailed results not shown). Overall, results from both analyses were consistent with the hypothesis that the hospital environment played a significant role in candidemia in Hamilton, Ontario, Canada. The summary

UPGMA

CA1
CA2
CA30
CA38
CA32
CA4
CA5
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CA34
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CA10
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CA41
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CA76
CA80
CA70
CA79
CA74
CA77
CA14
CA15
CA21

—— 0.01 changes

Fig. 1 Genetic relationships among independent strains of *Candida albicans* (CA) in this study.

information about strains in clusters within each of the four *Candida* species is presented in Table 4.

Discussion

In this study, *C. albicans* was found to be the most prevalent species isolated from patients with candidemia in Hamilton, Ontario, followed by *C. parapsilosis*, *C. tropicalis* and *C. glabrata* (Table 1). This result was largely consistent with several recent studies that showed an increasing proportion of non-*C. albicans Candida* species causing candidemia, most likely due to increased azole treatments that select for intrinsically more resistant species [1,4,6, 20–22]. However, none of the patients in our study had
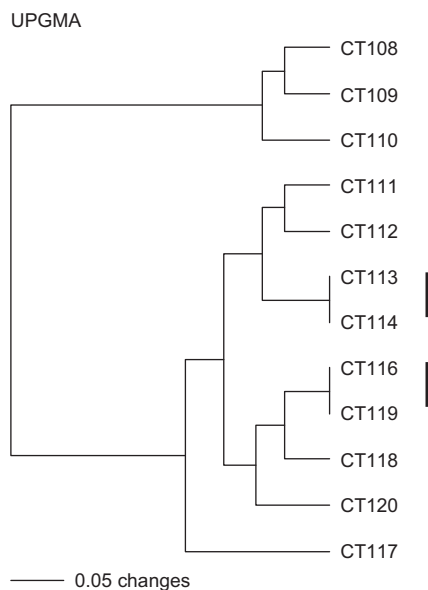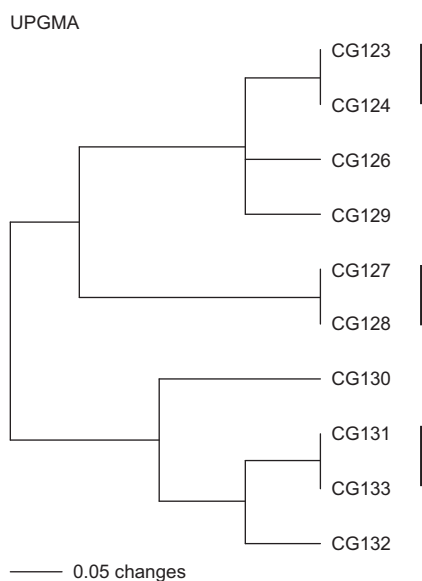
Fig. 2 Genetic relationships among independent strains of *Candida tropicalis* (CT) analyzed in this study.
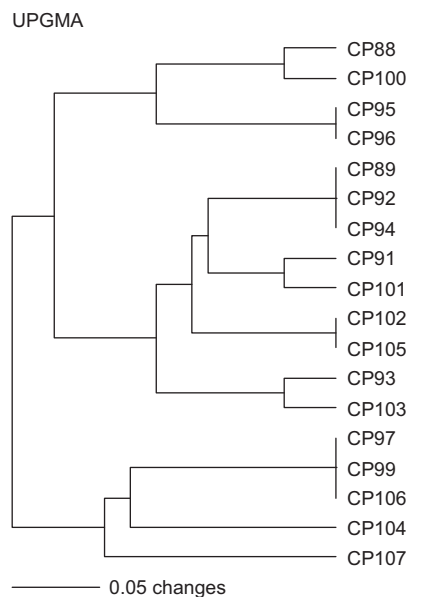
Fig. 4 Genetic relationships among strains of *Candida parapsilosis* (CP) analyzed in this study.

prior history of candidemia and very few had significant exposure to azoles. The lack of a prolonged selective pressure likely contributed to the slightly higher prevalence of *C. albicans* in our patient population than in most other samples from other countries/regions. Our observations were very similar to the recent studies conducted by Laupland *et al*. [23] in Calgary, Alberta, Canada and by St. Germain *et al*. [24] in Quebec, Canada.

Fig. 3 Genetic relationships among independent strains of *Candida glabrata* (CG) analyzed in this study.

The relative proportions of different yeast species causing candidemia as revealed here were also similar to those observed by Yamamura *et al*. [19] for the 1992–1994 surveyed samples in Canada. In that study, *C. albicans* accounted for 68.9% of all cases of candidemia in Canada, followed by *C. parapsilosis* (10.4%), *C. glabrata* (8.2%), and *C. tropicalis* (6.5%). In our investigation, the proportions of *C. albicans, C. parapsilosis, C. glabrata,* and *C. tropicalis* were 67.4%, 14.4%, 7.6% and 9.1%, respectively. Different from the previous retrospective study conducted by Yamamura *et al*. [19], the mean age of patients with candidemia in our study increased by about 10 years over the last decade. Since investigations by Laupland *et al*. [23] and St. Germain *et al*. [24] conducted elsewhere in Canada also indicated a gradual increase in the mean population age when compared to Yamamura *et al*. [19], this trend likely reflected the relative increase of the negative health effects suffered by seniors over that of the general population in Canada. For example, a large number of the patients admitted to hospitals in this study were the result of fractures (especially women) or solid tumors that often needed surgeries. Such surgeries were often accompanied by corticosteroids and the application of broad-spectrum antibiotics, both of which could favor the growth of opportunistic fungal pathogens such as *Candida* [25].

Previous studies conducted in Iceland focused on intra-ward strain clusters and showed that nosocomial transmission played a major role in causing candidemia in wards such as the ICU [4–6]. In this study, we broadened our scope and investigated both inter- and intra-ward clusters

Table 3 The mean pairwise genetic distance between strains isolated at different time intervals (all strain pairs vs. those < 90 d apart) within each of the four *Candida* species analyzed here.

| Species | Pair-wise genetic difference between all pairs of strains (%) | | Pair-wise genetic difference between strains isolated within 90 d of each other (%) | | T value | *P* value |
	n	Mean ± SD[*]	*n*	Mean ± SD		
C. albicans	3740	16.48 ± 6.23	1421	9.99 ± 3.17	162.09	< 0.001
C. glabrata	55	43.65 ± 23.68	17	9.89 ± 6.86	13.66	< 0.001
C. parapsilosis	190	28.14 ± 13.99	100	17.29 ± 7.92	27.71	< 0.001
C. tropicalis	103	32.21 ± 23.91	49	11.05 ± 5.74	13.55	< 0.001

[*]SD, standard deviation.

as opposed to only intra-ward clusters. Our analyses identified a likely strain transfer event between wards, even between hospitals. Another difference between this study and that of Ásmundsdóttir *et al.* [4] is the definition of a 'nosocomial cluster' where they used 95% genotype similarity as the cut-off for a strain cluster while we used 100% genotype similarity. If we relaxed our criterion to 95% genotype similarity, over 50% of the strains in our study would be in nosocomial clusters (data not shown).

To demonstrate that these clusters were not due to the lack of polymorphisms among the markers analyzed or due to the lack of diversity in the analyzed populations, we calculated the discriminatory power of the markers. Discriminatory power of a marker is the ability of the marker to differentiate between any two strains in a given population sample. A low discriminatory power would result in an overestimate of the number of strain clusters due to the grouping of different strains in the same cluster. In this study, the discriminatory power of the combined three markers was very high, close to 90% for each of the species (Table 2). This result and the retrospectively collected patient data helped ensure that the nosocomial clusters identified here were robust.
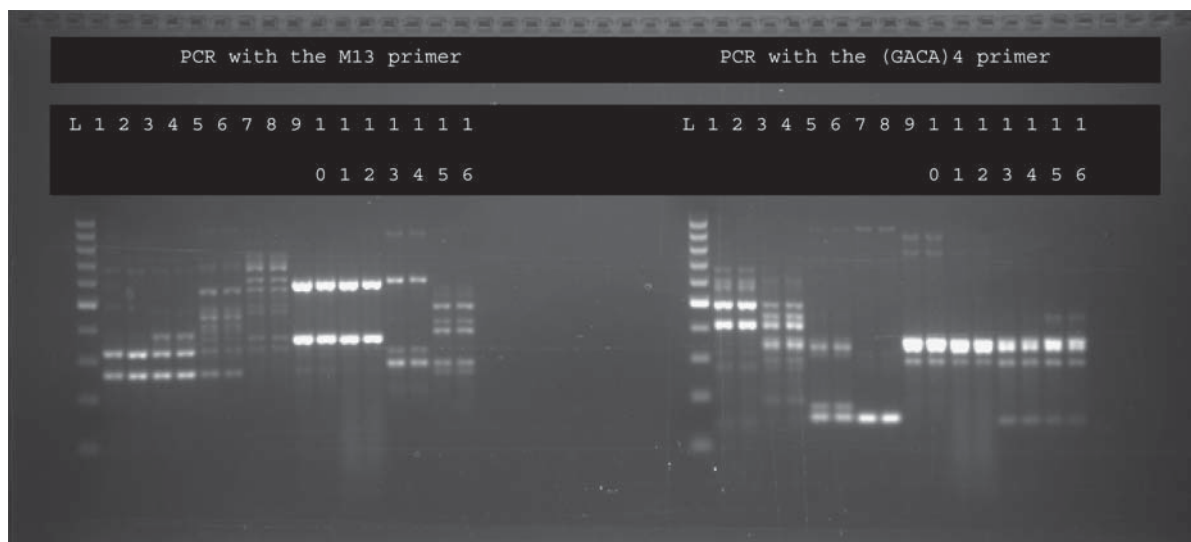
We observed a single *C. albicans* cluster containing clinical isolates from patients admitted in the ICU wards of two hospitals located about 10 km from each other. While strains CA5 and CA33 were found in the ICU wards of hospital A, strains CA34 and CA43 were found in the ICU wards of hospital B (Fig. 1). There are two possibilities for this observation. The first is the lack of genetic diversity between the exogenous strains of the analyzed

C. albicans population and that the clustering was purely by chance. However, the pairwise analysis of the 125 strains from different patients indicated that there was a high diversity among the strains of all four species of *Candida*, including *C. albicans*. The second hypothesis for the shared genotype between the two hospitals within 45 d was due to inter-hospital transmission. A possible route of such a transmission between hospitals could be through healthcare workers (doctors and nurses). Indeed, healthcare workers have been reported as likely agents of transmission for pathogens in several previous studies [9,10,26–28].

The observed genotype sharing across all four *Candida* species suggests that hospital environments (including healthcare workers) contributed to candidemia in Hamilton, Ontario. This hypothesis is further supported by our correlation analyses between genetic distance and temporal time difference, allowing us to determine the overall statistical significance of such clustering in the whole samples. The positive correlation observed between these two variables suggested that nosocomial infections contributed significantly to the observed candidemia in Hamilton hospitals. We found that for each of the four species, strains isolated closer to each other temporally were overall genetically more similar to each other as well. Indeed, our observations suggest that nosocomial sources likely caused repeated infections via strain replacement in one patient, who was affected by *C. parapsilosis*. In this patient, four blood culture isolates, CP92, CP94, CP102 and CP105 (Fig. 4) of *C. parapsilosis* were obtained, each one week apart from each other. The blood isolates CP92 and CP94, taken in the first two weeks clustered separately from

Table 4 Nosocomial clusters observed in the clinical isolates causing candidemia in Hamilton, Ontario, Canada, from 2005–2009.

| | No. isolates in clusters (% of total isolates) | Mean age of patients with strains in clusters (years) | No. strains in clusters (number of clusters in parenthesis) | | | |
			C. albicans	*C. tropicalis*	*C. glabrata*	*C. parapsilosis*
All patients	44 (33%)	66	26 (9)	4 (2)	6 (3)	8 (4)
Male patients	26	65	18	3	2	3
Female patients	18	67	8	1	4	5

Fig. 5 Banding patterns of independent strains present in nosocomial clusters using M13 and (GACA)$_4$ primers. Lanes 1–16 correspond to strains CA64, CA84 (a duplicate of CA64), CA85, CA86; CP92, CP94, CP102, CP105, CG123, CG124, CG131, CG133, CT115, CT116, CT121, and CT122, respectively. Strains CP92, CP94 and CP102 and CP105 were obtained from the same patient sequentially at one week intervals.

CP102 and CP105, the ones that were isolated in the last two weeks (Fig. 4). We hypothesized this might be due to two possible reasons: one was strain replacement and the second was mutation and microevolution. Microevolution has been observed to occur in *Candida*, especially in the presence of stress [18,29]. In our study, this patient was treated with caspofungin and fluconazole between the second and third strain isolations. However, microevolution typically refers to small changes within a clonal framework. In the specific case here, our fingerprinting analysis identified seven band differences between the two sets of strains when amplified with the M13 core primer and two band differences when amplified with the (GACA)$_4$ primer (Fig. 5). This magnitude of difference in the banding patterns suggested that strain replacement, not microevolution was likely responsible for the observed genotype change. Interestingly, the patient was a six-month old baby with a low birth weight. The reduced immunity at this age accompanied by the low birth weight condition might have played a significant role in acquiring the new strain in such a short period of time [21–22,30–33].

Previous studies have shown that the presence of a central line, solid tumor, diabetes, surgery and antibiotic therapy are major risk factors for candidemia. For example, a central line has been noted to be present in about 85% of the patients infected with *C. parapsilosis* [33,34]. In our study, among the 19 patients with candidemia caused by *C. parapsilosis*, all but one had a central line. *Candida parapsilosis* is known to produce biofilms over catheter surfaces leading to repeated infection of different patients by the same strain [34]. Similarly, diabetic patients are known to have compromised leukocyte function and immunity, leading to multiple abnormalities in host responses to microbial invasions. Urinary tract infections continue to be problematic in these patients because glucose in the urine provides an enriched medium. This could further complicate the issue if patients suffer from poor bladder emptying. Infections could ascend from the bladder to the kidney. Apart from people with diabetes, those with poor wound healing during post surgery periods are often at a high risk of developing candidemia from the endogenous and exogenous microflora [35].

In summary, we found that 33% of the patients sampled here from 2005–2009 in Hamilton, Ontario, were affected by strains sharing a genotype with at least another strain from unrelated hosts within a three-month period. Of the 18 clonal clusters, five were found in one hospital and 13 in another. The average age of intra-cluster patients with candidemia was 66 years (Table 4), about four years older than that of the mean age for all patients in this study. Our analyses suggest that the hospital environment could be a significant source of strains for candidemia and that measures should be taken in hospitals to reduce such infections.

Acknowledgements

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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This paper was first published online on Early Online on 5 January 2011.