Campylobacter concisus: an emerging pathogen of the gastrointestinal tract

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This chapter explores the role of Campylobacter concisus, as an emerging pathogen of the human gastrointestinal tract. This bacterium is a Gram negative curved rod that composes part of the gingival flora of the human oral cavity. The association of C. concisus with human periodontal diseases and gingivitis has been reported since the 1980s. However in this decade the focus on this species has shifted to its role in gastroenteritis in children and immunocompromised adults, in addition to its association with inflammatory bowel diseases. In particular the chapter focuses on the association of C. concisus with oral and intestinal infections, and on recent developments in applied molecular detection techniques to highlight the molecular diversity and virulence factors of this emerging pathogen.

Keywords: Campylobacter concisus; gingivitis; periodontitis; gastroenteritis; Inflammatory Bowel Diseases; hemolysin(s); adhesion; molecular detection; emerging pathogen; molecular diversity

1. Campylobacter concisus: The microorganism

Campylobacter concisus is a fastidious, hydrogen-requiring, slow growing organism that is found in the human oral cavity and occurs mostly in periodontal pockets of diseased gums. It has been characterised as an opportunistic microorganism associated with gingivitis, periodontitis and gastroenteritis [1, 2].

Tanner et al. [3] first described C. concisus (Latin concisus meaning concise) as small asaccharolytic, non-pigmenting gram-negative rods isolated from gingival crevices of persons with gingivitis and periodontitis. In 1984, Holdman et al. [4] renamed a group of organisms that derive their energy by reduction of fumarate or nitrate with formate or with hydrogen as Campylobacter concisus. These microorganisms were previously thought to be human isolates of "Vibrio succinogenes". This species was reported within a group called “anaerobic vibrios” to be small, Gram-negative, asaccharolytic rods, which grow in broth media supplemented with formate and fumarate [5], are motile with one or two polar flagella, and show a chemotactic response to formate in a concentration reported to be present in dental plaque [6].

The first isolation of C. concisus from a non-oral clinical specimen was reported in 1985 from a foot ulcer wound for a patient with diabetes mellitus [7]. However, until recently the pathogenic potential of this bacterium was uncertain as it has been identified in faecal samples from both healthy and diarrheic patients [1, 8-10]. In most diarrheal cases, C. concisus was isolated as the only potential intestinal pathogen, which implies that it is a primary pathogen. Since C. concisus is fastidious and has low biochemical activities, its identification is problematic by the conventional phenotypic techniques. In recent years the application of the “Cape Town protocol”, which involves membrane filtration onto antibiotic-free culture media [11], has enhanced the rate of C. concisus isolation from clinical samples. Also, the wider use of molecular detection techniques [12-13], has resulted in a higher number of reported C. concisus cases from gastric and extra-gastric infections.

Unlike most other Campylobacter spp., this bacterium does not have any known animal host and there are no reports on its isolation from healthy animals. A recent study to determine quantifiable levels of Campylobacter spp. shed from domestic pet dogs, using a culture-independent approach, reported the detection of C. concisus in faecal samples from diarrheic dogs, but failed to detect them in healthy dogs [14].

2. Campylobacter concisus of the human oral cavity

2.1. Campylobacter concisus as a part of oral cavity microbiota

A study by Macuch and Tanner [15] suggests that C. concisus, C. showae, C. curvus and Campylobacter X colonize the oral cavity more frequently than might be expected for transient species and may represent opportunistic pathogens under certain medical conditions. At least seven Campylobacter species have been identified from different subgingival sites, with C. rectus identified as a periodontal pathogen. Other Campylobacter spp. or taxa that have been isolated from oral sites include C. concisus, C. curvus, C. showae, C. showae-like, C. sputorum and Campylobacter X [15]. Campylobacter spp. other than C. rectus and C. gracilis have rarely been detected in periodontal samples, which could
be related to their presence below the detection limit of microbiological assays and to incomplete genotypic and phenotypic strain characterization [16].

2.2. The possible role of *C. concisus* in gingivitis and periodontitis

To date there is relatively little information on the exact involvement of *C. concisus* in periodontal disease, which may reflect difficulty in its isolation [17]. *C. concisus* has been linked to periodontal disease since the early 1980's [3, 18]. The species has been demonstrated in gingivitis in young adults. An investigation on the composition of the subgingival microbiota in children with primary dentition aged 4-5 years showed that *C. concisus* was present in low numbers generally and was isolated in greater numbers around molars than incisors [19]. In children aged 7-8 years with a mixed dentition, *C. concisus* was found more frequently in plaque from permanent teeth than plaque from deciduous teeth [20], and it was associated with bleeding gum sites in both groups [19-20]. This organism has been identified as a pathogen in early-onset forms of periodontal disease and has been associated with progression of the disease especially in bleeding sites [20-22]. *C. concisus* has also been associated with the progression of periodontitis in adults [23-24], and also patients with periodontal disease showed a greater antibody response to this bacterium compared to healthy subjects [25]. *C. concisus* was grouped into one of the six successional complexes that are believed to be involved in periodontal diseases [26].

3. *Campylobacter concisus* from non-oral origins

3.1. Etiology and prevalence of *C. concisus* in gastroenteritis

*C. concisus* has been linked to gastroenteritis, particularly in infants from 0-35 months of age and has been isolated (mainly by culture filtration technique) from children with diarrhoea in Europe, Australia and South Africa [8-11]. The reported isolation rates for *C. concisus* varies widely between laboratories which could be influenced by isolation and identification methods, geographical factors, sources and routes of transmission, as well as numbers of faecal samples tested and differences in study population regarding age group and health conditions [27]. The isolation rate of *C. concisus* from stool samples of paediatric patients with diarrhoea, was reported to be 5% of the total samples tested over a ten year period at Cape Town in South Africa, the second highest rate after *C. jejuni*, when the stool filtration technique on an antibiotic free blood agar was introduced [2]. However, when a similar technique was used to isolate H₂-requiring *Campylobacter* spp. at the Royal Children’s Hospital (RCH) in Melbourne, Australia, an isolation rate of 3% was reported for *C. concisus*. Most of the patients were reported to be 2-30 months of age with gastrointestinal symptoms including diarrhoea, vomiting, fever, and abdominal pain [28, 29].

A study undertaken in Copenhagen, Denmark [8] reported a total of 52 *C. concisus* strains isolated from 1,376 diarrheal cases (>3%), particularly in young children (<24 months) and the elderly (> 60 years). These finding were followed by a study from another Danish research group [30] on the prevalence of *C. concisus* in diarrhoea of immunocompromised patients. It was reported that *C. concisus* was the most prevalent *Campylobacter* spp. isolated, being responsible for 49% (110/224) of all campylobacter isolates in immunocompromised patients, and that the isolation rate was higher in late summer with a smaller peak in spring [30]. Seasonal variations and peak patterns in spring and summer were similarly found in gastroenteritis cases caused by *C. concisus* in Australian children at a study conducted at RCH in Melbourne (P. Ward, unpublished).

3.2. *C. concisus* in Crohn’s disease patients

A recent study in Sydney, Australia [31] on 114 colonic biopsies from children with Crohn’s disease (CD) attending Sydney Children's Hospital, found that a significantly higher percentage of *Campylobacter* species (82%), and in particular *Campylobacter concisus* (52%), were detected with high titre of antibody against *C. concisus* as compared with controls. This finding is of particular significance given that the pathogenic potential of *C. concisus* and other non-jejuni *Campylobacter* species has recently begun to be recognised [31, 32].

3.3. *C. concisus* from extra-oro-intestinal infections

*C. concisus* was recently detected in the synovial fluid of patients with campylobacter-associated reactive arthritis [33]. Reverse transcription PCR amplification of specific 16S rRNA sequences was applied on synovial fluids from arthritis patients, which revealed the presence of transcriptionally active skin and gut commensals including two different *C. concisus* strains. In addition *C. concisus* has been detected by PCR in 4 of 7 endoscopic biopsy samples from patients with Barrett’s esophagitis (BE), but in none of the controls [34]. A more recent study on cases of extra-oro-intestinal abscesses reported *C. concisus* detection in a 65-year-old man with a history of maxillary sinus carcinoma, whom later developed a brain abscess due to polymicrobial flora [35]. As *Campylobacter* spp. including *C. concisus* are rarely
isolated from extra-oro-intestinal origins, the pathogenic role of this organism in such polymicrobial infections is to be elucidated.

4. Isolation and identification of *Campylobacter concisus* in clinical samples

4.1. Culture and Microscopy

The filtration method combined with selective culture [8] or growth on an antibiotic free medium [2], are the most common methods for the isolation of this bacterium from stool samples of enteritis patients.

All *C. concisus* strains are slower in their growth than *C. jejuni* and they require hydrogen-enriched environment, in addition they grow better at 37°C than at 42°C. Faecal material or other samples can be cultured by preparing a 1:2 to 1:10 suspensions in phosphate buffered saline (pH 7.4) or in heart infusion broth. Four or 5 drops of the suspension are placed on a 0.65µM pore size cellulose acetate filter placed on the surface of a Petri dish of Columbia blood agar base containing 5% horse or sheep blood. After the fluid has soaked through, within approximately 10 min, the filter is then removed and discarded. Once any remaining visible suspension has soaked into the agar the plates should be incubated at 37°C in an atmosphere of 7% hydrogen, 7% carbon dioxide 7% oxygen and the balance of nitrogen. This can be achieved either by using the evacuation replacement procedure by evacuating an anaerobic jar to approximately -0.7 bar and then re-gassing to atmospheric pressure with a gas mixture of 10% hydrogen, 10% carbon dioxide and a balance nitrogen, or by the use of an anaerobic gas pack in an anaerobic jar without a catalyst (if using gas packs that require catalyst). The plates should be incubated for 3-5 days before the jar is opened.

*C. concisus* colonies are small (1-2 mm), round, entire, greyish and semitranslucent. Microscopy of wet mounts of this bacterium in PBS or heart infusion broth reveals very small, slightly curved rods with rapid darting motility. Gram staining shows small fine curved to spiral Gram negative rods. Like other *Campylobacter* spp. *C. concisus* can form long rods and may also be found in coccoid forms as indicated in (Fig.1).

![Fig. 1](image)

**Fig. 1** Gram-stained smear for a 5 days old culture of *Campylobacter concisus*, presenting both the normal short curved, and the long curved bacterial cells from the same colony. Magnification 1000x [9].

4.2. Conventional phenotypic identification

Suspected *C. concisus* colonies can be identified by conventional phenotypic and biochemical tests for *Campylobacter* spp. including colony morphology, organism motility, organism morphology by Gram stain, oxidase, catalase, dependency on hydrogen for growth, H$_2$S production, indoxyl acetate hydrolysis, DNase production, susceptibility or resistance to specific antibiotics, hippurate hydrolysis, nitrate reduction and growth on MacConkey agar [10, 36, 37].

Sensitivity to cephalothin and nalidixic acid, the growth of cultures at 25°C and 42°C, and colony colour, are of little use in differentiation between *C. concisus* and *C. mucosalis* [38], and to differentiate strains from both species. A diagnosis based only on biochemical reactions and susceptibility tests misidentified a *C. concisus* strain, isolated in almost pure culture from stool of a young male with a chronic lymphatic leukaemia, as *C. mucosalis*. The isolation was later identified as *C. concisus* by conducting a 16S rRNA sequencing [39].

4.3. Molecular Detection and Characterisation

In 1989 Vandamme *et al.* [1] used SDS-PAGE protein profiles, immunotyping and DNA:DNA hybridization, to identify the 22 *C. concisus* EF group strains isolated from patients with gastroenteritis. These strains had a DNA binding value of at least 42% with the *C. concisus* type strain, showing a degree of genomic heterogeneity. This study concluded that *C. mucosalis* is more closely related to *C. concisus* than any other *Campylobacter* spp. [1]. However later molecular studies indicated that the H$_2$-requiring *Campylobacter* species appear to be closely related phylogenetically [40, 41]. *C. concisus, C. showae, C. rectus, C. curvus, C. gracilis, C. spotorum* and *C. hominis* all
belong to the first distinct group of the 16S rDNA sequences of *Campylobacter* spp. phylogenetic tree as determined by neighbour-joining analysis [41].

The first *C. concisus*-specific PCR assay, based on a target sequence of 23S rDNA was developed by Bastyns *et al.* in 1995 [12]. Subsequently, Engberg *et al.* [8] reported consistently obtaining a PCR product of 308 bp for the amplified gene fragment from type strains of *C. showae* and *Wolinella succinogenes* in preliminary set up experiments. Matsheka *et al.* [13] indicated too that this method did not identify *C. concisus* consistently, because of the genotypic heterogeneity within the species, and reported developing a more reliable and rapid PCR assay which is currently regarded more specific for the molecular detection of *C. concisus* by using primers annealing to the extremities of a 1.6kb DNA fragment isolated from a *C. concisus* genomic library. This PCR assay was considered specific for *C. concisus* as specific products were not obtained from any other *Campylobacter* spp. [13]. Gorkiewicz *et al.* [42] suggested that partial 16S rRNA gene sequencing is an effective and rapid procedure for the specific identification of *Campylobacter* spp. including *C. concisus*. Hence, as the complete genome sequence of *C. concisus* 13826 (NCBI Reference Sequence: NC_009802.1) has been deposited in the Gene Bank databases in late 2007, many PCR detection assays have been developed recently for the molecular detection of this species in clinical samples [33].

4.4. Antimicrobial Resistance

There is a scarcity of reports on susceptibility testing and of resistance patterns of *C. concisus*. There is also a lack of a standard validated method for simple use in a diagnostic laboratory. Disc diffusion testing is not reliable for this slow growing organism and the dilution antimicrobial test is too cumbersome. Two recent studies successfully used E-tests to generate some MICs for *Campylobacter* spp. [43, 44]. Unfortunately, there are no interpretive data and breakpoints for determining resistance and susceptibility of *C. concisus* in the Clinical and Laboratory Standards Institute (CLSI) approved standards. Aabenhus *et al.* [43] reported resistance rates among 109 isolates of *C. concisus*, which were 2% for ampicillin, 5% for ciprofloxacin, 0% for ceftriaxone, 7% for erythromycin and 3% for tetracycline. Vandenberg *et al.* [44] tested the antibiotic resistance of 20 *C. concisus* strains. All had a MIC of ≤ 1 mg ampicillin/L, 100% had gentamicin MICs of ≤ 4 mg/L, and 95% had ciprofloxacin MICs of ≤ 1 mg/L (1 had a MIC of 32 mg/L). Tetracycline and erythromycin MICs were ≤ 4 mg/L in all isolates. Only 80% were reported as resistant to naladixic acid with MICs of 32 or more. This suggests that a reduced MIC to ciprofloxacin would be expected and hence potential treatment failure if ciprofloxacin was used to treat infection.

4.4.1. Should *C. concisus* be treated with antibiotics?

Although there are recent reports of *C. concisus* involvement in periodontal disease, diarrhea and Crohn’s disease [15-16, 30-35, 45], its isolation in many cases is not associated with enteric disease. Thus, more data and evidence are needed before the role of antibiotics can be assessed. If antibiotics are used, particularly in the immunocompromised it is most likely that agents found to be successful in treating of other *Campylobacter* spp. would be successful also with *C. concisus*. Therefore, it would be wise to check ciprofloxacin MICs before initiating treatment and to check clearance and MICs in isolates where clinical response is slow. As a high proportion of *C. concisus* isolates are resistant to naladixic acid, it may be that ciprofloxacin resistance or poor response to such therapy would result from accumulating mutations in the *gyrA* gene. It was reported [46] that the use of veterinary specific fluoroquinolones in chickens generated a rapid increase in the ciprofloxacin MICs of *C. jejuni* (from 0.250 mg/mL to 32 mg/mL). This increase appeared within the treatment time frame and persisted long after treatment was stopped [46]. Therefore, as fluoroquinolones are commonly used to treat patients with *Campylobacter* spp. infections, the emergence of resistant strains will limit the therapeutic usefulness of these drugs.

5. *Campylobacter concisus*: a heterogenous species

Little is known about *C. concisus* mode of transmission, reservoir, and pathogenesis due to the lack of well established typing procedures and virulence related studies [47]. *C. concisus* is known to be heterogeneous; therefore a definitive identification of this species is complex because of its phenotypic diversity. The lack of well-documented methods that can effectively discriminate *C. concisus* genotypes, as well as the lack of extensive studies for virulence factors has hindered the findings on whether *C. concisus* strains colonising the oral cavity represent a single genotype that is also recovered from cases of diarrhoea and from healthy individuals [15, 27, 37]. Protein electrophoresis and DNA-DNA hybridization revealed that *C. concisus* is a heterogeneous species with many genotypic subgroups.

5.1. Protein profiles of *C. concisus* clinical isolates:

SDS-PAGE protein profiles were first used to highlight species differences between *C. concisus* and other small asaccharolytic, non-pigmenting Gram-negative rods of the human oral cavity by Tanner *et al.* in 1986 [48]. Analysis of SDS-PAGE protein profiles of 19 *C. concisus* RCH clinical strains isolated from gastroenteritis cases in children in addition to reference strains ATCC 51561 and 51562 was conducted by our team [29]. The study assigned these strains
into more than five groups according to their protein profiles, and concluded that the protein profiles of whole cell lysates (WCL) and outer membrane proteins (OMPs) for the strains were divergent, but they had no similarity with the protein profiles of *C. mucosalis* ATCC 43264 [29]. The WCL protein profiles (Fig. 2 a) and OMP profiles (Fig. 2 b) for *C. concisus* clinical strains (Lanes 2-9, Fig. 2 a & b) and *C. mucosalis* ATCC 43264 (Lane 1, Fig. 2 a & b) demonstrate the diversity of the protein profiles within *C. concisus* isolates, yet these profiles are distinguishable from *C. mucosalis* ATCC 43264 profile. The figure also shows the significant similarity between the protein profiles of at least 3 *C. concisus* clinical strains (Fig. 2, lanes 5-7, in a, and 4-6 in b).

5.2. Molecular typing of *C. concisus* strains

Understanding the epidemiology of *C. concisus* was hampered by the lack of an established genotypic identification tool. Only limited genotyping studies have been carried out on *C. concisus*. At present, this species is known to comprise at least four genomospecies, which are phenotypically indistinguishable, but genetically divergent by DNA hybridization, AFLP analysis, PFGE, and by PCR amplification [1, 43, 37, 49, and 9 respectively]. A modification of the PCR amplification of the 23S rDNA region in *C. concisus* [12] assigned 21 *C. concisus* strains into two molecular groups (genomospecies) [29]. This modified 23S rDNA PCR method was applied on 39 *C. concisus* isolates from Denmark and the strains were also assigned into 2 definitive genomospecies [37]. The ratio of *C. concisus* isolates from Australia assigned to the first group (genomospecies A) was 71.8% as compared to 33.3% of the isolates from Denmark. And the ratio for the second group (genomospecies B) within the isolates from Australia was 28.2% as compared with 66.7% for the isolates from Denmark (29, 37 respectively). These results indicate that a true difference in geographical distribution of *C. concisus* genomospecies related to gastroenteritis might exist, which needs to be further investigated.

Aabenhus *et al* [43] used Amplified Fragment Length Polymorphism Analysis (AFLP) to investigate the genetic diversity of the species, and the results were correlated with clinical data [43]. All *C. concisus* strains gave unique AFLP profiles, and numerical analysis of these data distributed the strains among four genomospecies. The strains from the 2nd genomospecies were more frequently isolated from immunocompetent patients and/or patients without concomitant infections that presented with fever, chronic diarrhoea, and gut inflammation. It was indicated too that only strains from this genomospecies were correlated with bloody diarrhoea [43]. This was also confirmed when the same AFLP typing system was applied on South African isolates from paediatric gastroenteritis patients (Stephen On, personal communication). The current AFLP analysis data show that *C. concisus* contains at least four distinct genomospecies that may exhibit differences in their spectra of virulence potential [43]. The occurrence of bloody diarrhoea in cases with a particular genomospecies, suggest that a specific toxin which is produced by these strains may be involved.

![Fig. 2](image)

**Fig. 2** SDS-PAGE protein profiles for *C. concisus* whole cell lysates (WCL) in a, and outer membrane proteins (OMPs) in b. The protein profiles in lane 1 are for *C. mucosalis* (ATCC 43264). Protein profiles in lanes 2-9 are for *C. concisus* clinical strains isolated from children with diarrhoea in Melbourne, Australia [9].
6. Virulence factors in *Campylobacter concisus*

To date, only limited studies on the potential pathogenicity of this species have been conducted [9]. Adhesion and invasion assays performed on four of RCH *C. concisus* isolates showed that three of the four strains were adhesive and invasive to INT407 cell line [28]. These four isolates were among other RCH clinical strains reported to be haemolytic on different types of erythrocytes [29, 50]. CDT-like effect on Vero cells was also reported in 90% of 39 *C. concisus* isolates from Danish patients with diarrhoea [37].

6.1. Hemolysins of *C. concisus*

Cell- associated and secreted hemolytic activities have been reported in *C. concisus* clinical isolates [29, 50]. Both types of hemolysins have been reported in other pathogenic *Campylobacter* spp. such as *C. coli* and *C. jejuni* [51]. The detection and characterisation of a stable, cell-associated hemolysin was reported in 21 *C. concisus* clinical strains [29, 50]. This hemolysin was characterised as a calcium-dependent, cytolytic, outer-membrane phospholipase A (OMPLA) [9]. The hemolytic fraction of the extracted membrane-bound phospholipase A induced vacuolation and cytolysis of Chinese Hamster Ovary (CHO) cell line (Fig. 3 b & c respectively).

![Fig. 3](image-url) Phase contrast photomicrographs for Chinese Hamster Ovary (CHO) cell line treated with a crude haemolytic extract (HE) of *C. concisus*. Cells were cultured in a 24-well plate until they reached confluent stage in (a). The confluent growth was then treated with diluted HE in (b), or with concentrated HE in (c). After incubation at 37°C under a 5% CO₂ atmosphere, cells were examined by phase-contrast microscopy at 16 h. *C. concisus* HE caused detachment of the confluent layer and induced vacuolation and cytolysis of CHO cells (b & c respectively).

Further investigations to detect possible genes related to the membrane-bound hemolysin in *C. concisus* resulted in the identification of a *pldA* gene, the structural gene encoding for phospholipase A (accession no. AJ786391). The nucleotide sequences of the *pldA* gene in different *C. concisus* strains had >98% similarity with the *pldA* gene of *C. coli* [29, 50], and the nucleotide sequence of the *pldA* gene is highly conserved in *Campylobacter* spp. indicating interspecies conservation of this gene. This is not unexpected, as the *pldA* gene is highly conserved in other Gram-negative bacteria too [52]. When the nucleotide sequences of the flanking regions of the *pldA* gene were analysed, it revealed that the *pldA* gene in *C. concisus* is located upstream of the *ceuB* gene [9]. A similar structure of the *pldA* gene upstream of the *ceuB* and the *ceuC* genes which are associated with the enterochelin transport system has been reported in both *C. coli* and *C. jejuni* genomes. However, no homolog for the *pldA* gene was found in the complete genome sequence of *C. concisus* 13826 complete genome (Accession NC_009802), indicating that the *pldA* gene is missing in this strain, probably by deletion at an earlier evolutionary stage, or perhaps the Australian isolate/s has acquired the *pldA* gene from a related species in more recent times.

The 3D structure for the *C. concisus* PLA molecule in (Fig. 4 a) indicated that it has a β-barrel structure with a significant resemblance to the PLA protein molecule of *C. coli* (Fig. 4 b) and to the 12-β-stranded architecture proposed for OMPLA molecule of *E. coli* (Fig. 4 c) [9, 50]. Recent studies have indicated a possible role of *pldA* gene product in bacterial colonisation and virulence of *C. coli* and *C. jejuni* pathogenic strains [53, 54]. Similar research with a *pldA* mutant in *Helicobacter pylori* suggested that the *H. pylori* phospholipase has a role in colonisation of the gastric mucosa and possibly tissue damage after colonisation [55].

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A labile secreted hemolytic activity was detected in fresh cultures of *C. concisus* clinical strains. This hemolytic effect was neutralised by incubating the hemolytic extract (HE) with *C. concisus* specific antiserum raised against whole cell extracts of a *C. concisus* clinical strain [50]. The influence of iron on hemolytic activity was investigated to determine the possible presence of iron-regulated hemolysins in *C. concisus* as previously reported in other Gram negative bacteria. Ferrous ions had a significant effect on hemolytic activity of *C. concisus* [50]. Hemolysin synthesis is known to be regulated by iron in Gram negative pathogens such as *C. jejuni* and *V. cholerae* [56-57], therefore the presence of iron-regulated hemolysin(s) in *C. concisus* suggests a potential role for this hemolysin as a virulence factor in the disease caused by this microorganism. Furthermore, the neutralisation of the secreted hemolytic activity when it was incubated with *C. concisus* polyclonal antiserum indicated the immunogenic effect of the hemolysin(s) [9, 50].

The sequencing of *C. concisus* hemolytic inserts from *C. concisus* genomic library identified genes similar to those present in other *Campylobacter* spp. but with no relation to hemolytic activity [50]. The nucleotide sequences of the *hemA* and the *proS* genes (Accession FM178561) have 82% similarity to the genome sequence of *C. curvus* 525.92 (Accession CP000767). The detection of both secreted and membrane-bound hemolytic activities in *C. concisus* indicated the presence of certain virulence factors in this opportunistic pathogen. Furthermore, the determination of gene clusters with nucleotide sequences similar to genes that are known to influence hemolytic activity and virulence in other *Campylobacter* spp., in addition to the full characterisation of the *C. concisus* pldA gene and its role in the production of the hemolytic phospholipase A activity indicate the possible pathogenic role of this bacterium in gastroenteritis.

7. Conclusion

The emergence of *C. concisus* as a human pathogen has been slow. However, it is now becoming more obvious that this bacterium can colonise people, and has a number of virulence factors that are shared with other *Campylobacter* spp. Hence, with reports of disease associations, further clinical and laboratory research is needed to clearly define the role that *C. concisus* and some of its cellular components might have in relation to the colonisation and pathogenesis.

References


