Post–COVID-19 Emergence and Spread of Hypertransmissible *Cryptosporidium hominis gp60* Subtype IfA12G1R5, Spain

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COVID-19 pandemic containment measures in 2020 selectively altered established *Cryptosporidium hominis* anthroponotic transmission in Spain. Rapid emergence and expansion of hypertransmissible human-adapted *gp60* subtypes such as IfA12G1R5 and, less markedly, IbA13G3 followed. Conversely, transmission of the largely zoonotic *C. parvum* remained comparatively stable, yielding a dual epidemiologic scenario in this country.

Cryptosporidiosis is a public health concern in Europe; outbreaks have been linked to contaminated drinking water, recreational water, and fresh produce (*1*,*2*). In 2020, the European Union reported 1.7 confirmed cases/100,000 population (https://www.ecdc.europa.eu/en/publications-data/cryptosporidiosis-annual-epidemiological-report-2020), although the true burden is likely underestimated because of underdiagnosis and underreporting.

The COVID-19 pandemic and associated nonpharmaceutical interventions altered the epidemiology of gastrointestinal pathogens (*3*). The effects of those measures on *Cryptosporidium* species varied, as shown in time-series analyses comparing prepandemic and postpandemic incidence of cryptosporidiosis and molecular data from countries in Europe (England, Scotland, and Wales) and New Zealand (*4*–*6*). Furthermore, a postpandemic study in Spain of young children with diarrhea demonstrated an interruption in the transmission of *C. hominis*, but not *C. parvum* (*7*). We collated prepandemic and postpandemic molecular data from published literature and from multicenter, nonoutbreak studies to investigate the molecular epidemiology of *Cryptosporidium* infection in Spain after the interruption in transmission of *C. hominis* and the relaxation of COVID-19 containment measures in 2020.

The Study

We searched PubMed, Web of Science, and Scopus databases for molecular studies on human cryptosporidiosis conducted in Spain published during January 2010–December 2020 (Appendix, https://wwwnc.cdc.gov/EID/article/32/12/26-1007-App1.pdf). Search terms included *Cryptosporidium*,

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Table 1. Diversity and frequency of *gp60* families of *Cryptosporidium hominis* and *C. parvum* from prepandemic clinical samples, Spain, 2013–2019

		C. hominis, n = 332					*C. parvum*, n = 57				
Hospital	Region	Ia	Ib†	Id	Ie	If‡	IIa	IIc	IId	IIn	Total
Gran Canaria	Canarias	0	16 (16)	0	0	0	0	2	4	0	22
Unknown	Canarias	0	2 (2)	0	0	0	0	0	2	0	4
Santa Bárbara	Castilla-La Mancha	0	0	0	0	0	0	0	0	0	0
León	Castilla-León	0	1 (1)	0	0	0	0	0	0	0	1
Medina del Campo	Castilla-León	0	1 (1)	0	0	0	0	0	0	0	1
Clinic	Cataluña	0	5 (5)	0	0	1 (1)	0	0	1	0	7
Vall d´Hebron	Cataluña	0	6 (6)	0	0	0	0	0	0	0	6
Elche	Comunidad Valenciana	0	2 (2)	0	0	0	0	0	0	0	2
La Fe	Comunidad Valenciana	0	0	0	0	0	0	0	0	0	0
San Pedro*	La Rioja	0	59 (57)	0	0	0	3	0	3	0	65
12 de Octubre*	Madrid	0	11 (9)	0	1	0	3	0	0	0	15
Fundación Jiménez Díaz	Madrid	1	7 (6)	0	0	0	1	0	0	0	9
La Paz	Madrid	0	3 (3)	0	0	0	1	0	0	0	4
Puerta de Hierro*	Madrid	1	131 (127)	0	2	0	15	0	4	0	153
Ramón y Cajal	Madrid	0	3 (3)	0	0	0	0	0	0	0	3
Severo Ochoa*	Madrid	0	59 (57)	0	5	0	8	0	5	0	77
Unknown	Unknown	0	15 (15)	0	0	0	3	0	2	0	20
Total		2	321 (310)	0	8	1 (1)	34	2	21	0	389

*Hospitals participating in the dedicated multicenter nonoutbreak study. Other samples were routinely submitted for genotyping to the National Reference Laboratory at the Spanish National Centre for Microbiology from 7 regions.
†Number of samples characterized as *gp60* subtype IbA10G2 indicated in parentheses.
‡Number of samples characterized as *gp60* subtype IfA12G1R5 indicated in parentheses.

human, *hominis*, *parvum*, *gp60*, subtype, and Spain. We identified 7 studies reporting molecular data on *Cryptosporidium* from laboratory-confirmed clinical samples collected in Spain during 2000–2016; a total of 806 isolates were characterized (Appendix Table). Among *C. hominis* (76.1%), subtype family Ib predominated (90.7%); subtype IbA10G2 accounted for 99.6% of isolates. Among *C. parvum* (24.0%), subtype family IIa predominated (87.1%), followed by IIn (7.3%) and IId (5.2%).

During December 2013–December 2019, we collected *Cryptosporidium*-positive clinical fecal samples routinely submitted for genotyping to the National Reference Laboratory at the Spanish National Centre for Microbiology from 7 regions (Table 1). We obtained additional prepandemic samples through a dedicated multicenter nonoutbreak study across 4 tertiary hospitals in 2 regions (Table 1). During March–December 2023, we collected postpandemic *Cryptosporidium*-positive clinical samples through a dedicated multicenter nonoutbreak study across 8 tertiary hospitals in 2 regions (Table 2). Upon receipt, all samples were subjected to confirmatory testing and genotyping at the *gp60* marker in accordance with established protocols and current subtype nomenclature recommendations (*7*,*8*). We considered only samples identified as *C. hominis* or *C. parvum* in our analysis.

Our analysis included 389 prepandemic clinical samples (Table 1). Among *C. hominis* (85.3%), subtype family Ib predominated (96.7%); subtype IbA10G2 accounted for 96.6% of isolates. Among *C. parvum* (14.7%), subtype family IIa was most common (59.6%), followed by IId (36.8%) and IIc (3.5%).

Our analysis included 126 postpandemic clinical samples (Table 2). Among *C. hominis* (96.0%), the most common subtype families were If (70.2%) and Ib (22.3%). All If isolates belonged to subtype IfA12G1R5, whereas IbA10G2 represented 7.4% and IbA13G3 represented 88.9% of isolates within subtype family Ib. *C. parvum* accounted for the

Table 2. Diversity and frequency of *gp60* families of *Cryptosporidium hominis* and *C. parvum* from postpandemic clinical samples genotyped at the National Reference Laboratory, Spain, 2023

		Cryptosporidium hominis, n = 121					*C. parvum*, n = 5				
Hospital	Region	Ia	Ib*	Id	Ie	If†	IIa	IIc	IId	IIn	Total
Arnau de Vilanova	Cataluña	1	1 (0)	0	0	0	0	0	0	0	2
Belltvitge	Cataluña	0	1 (0)	0	0	11 (11)	0	0	0	0	12
Clinic	Cataluña	0	2 (1)	0	0	0	0	0	0	0	2
Germans Trias i Pujol	Cataluña	0	0	0	0	0	0	0	0	0	0
Vall d´Hebron	Cataluña	3	18 (1)	1	1	41 (41)	2	0	0	0	66
Fundación Alcorcón	Madrid	1	3 (0)	0	1	12 (12)	2	0	0	0	19
La Paz	Madrid	0	2 (0)	0	1	17 (17)	0	0	0	0	20
Ramón y Cajal	Madrid	0	0	0	0	4 (4)	1	0	0	0	5
Total		5	27 (2)	1	3	85 (85)	5	0	0	0	126

*Number of samples characterized as *gp60* subtype IbA10G2 indicated in parentheses.
†Number of samples characterized as *gp60* subtype IfA12G1R5 indicated in parentheses.

Table 3. Diversity and frequency of *gp60* family subtypes of *Cryptosporidium hominis* and *C. parvum* from all clinical samples genotyped at the National Reference Laboratory, Spain, 2013–2023

Species and family	Subtype	2013	2014	2015	2016	2017	2018	2019	2023	Total	GenBank accession no.
C. hominis											
Ia	Ia	0	0	0	0	0	0	0	1	1	*
	IaA12	0	0	0	0	0	0	0	3	3	PZ808827
	IaA13	0	0	0	0	0	1	0	1	2	PZ808828
	IaA22	0	0	1	0	0	0	0	0	1	PZ808829
Ib	Ib	0	0	2	0	0	0	0	0	2	*
	IbA10G2	8	63	52	0	38	76	73	2	312	PZ808830
	IbA10G3	0	0	1	0	0	0	0	0	1	PZ808831
	IbA12G3	0	0	0	0	2	4	0	1	7	PZ808832
	IbA13G3	0	0	0	0	0	2	0	24	26	PZ808833
Id	IdA16	0	0	0	0	0	0	0	1	1	PZ808834
Ie	IeA11G3	0	2	1	0	1	1	1	3	9	PZ808835
	IeA12G3	1	1	0	0	0	0	0	0	2	PZ808836
If	IfA12G1R5	0	0	0	0	1	0	0	85	86	PZ808837
C. parvum											
IIa	IIaA15G2R1	0	5	4	0	7	3	4	4	27	PZ808838
	IIaA16G1R1	0	0	0	0	0	1	0	0	1	PZ808839
	IIaA16G2R1	0	0	0	0	1	0	0	1	2	PZ808840
	IIaA17G2R1	0	0	0	2	0	2	2	0	6	PZ808841
	IIaA19G4R1	0	1	0	0	0	1	0	0	2	PZ808842
	IIaA22G2R1	0	0	0	0	0	1	0	0	1	PZ808843
IIc	IIcA5G3	0	0	0	0	0	1	1	0	2	PZ808844
IId	IIdA15G2	0	0	0	0	2	0	0	0	2	PZ808845
	IIdA17G1	0	0	0	0	0	0	2	0	2	PZ808846
	IIdA18G1	1	1	0	0	0	1	0	0	3	PZ808847
	IIdA18G2	0	1	0	4	0	0	0	0	5	PZ808848
	IIdA19G1	0	0	0	0	1	0	0	0	1	PZ808849
	IIdA22G1	0	0	0	0	0	1	1	0	2	PZ808850
	IIdA22G2	0	0	0	0	0	1	0	0	1	PZ808851
	IIdA23G1	0	0	0	0	0	2	1	0	3	PZ808852
	IIdA26G1	0	0	0	0	0	1	0	0	1	PZ808853
	IIdA29G1	0	0	0	0	0	1	0	0	1	PZ808854
Total		10	74	61	6	53	100	85	126	515	

*GenBank accession numbers were not provided because sequence quality was insufficient to identify the subtype.

remaining 4.0% of isolates, all of which belonged to subtype family IIa.

The distribution of *C. hominis* subtypes in 2023 differed markedly from that observed during 2000–2019, both in diversity (10 vs. 2–5 subtypes) and frequency rates, as determined by comparison to clinical samples genotyped at the National Reference Laboratory and deposited to GenBank during 2013–2023 (Table 3). Subtype IfA12G1R5 accounted for 67.5% of cases despite being detected only once previously, whereas the historically predominant subtype IbA10G2 declined dramatically from 79.7% to 1.6%. *C. parvum* was rarely detected in 2023.

Conclusions

Before the COVID-19 pandemic (2000–2019), *C. hominis* was the predominant species in Spain, accounting for ≈76%–85% of cases; subtype family Ib was overwhelmingly dominant (91%–97%) (Table 1; Appendix Table). Within family Ib, IbA10G2 was most frequently identified across multiple studies and settings (97%–99%), suggesting a well-established and stable anthroponotic transmission network. *C. parvum* accounted for a smaller percentage of infections; family IIa predominated, particularly IIaA15G2R1 (Table 1; Appendix Table). That pattern is consistent with ongoing zoonotic transmission linked to livestock or wildlife exposure.

The COVID-19 pandemic appears to have altered this equilibrium. Evidence from several countries indicates that nonpharmaceutical interventions disproportionally affected *C. hominis*, whose transmission relies primarily on person-to-person contact and common-source exposures. Indeed, postpandemic reductions or even interruptions in *C. hominis* transmission have been reported in England and Wales (*3*,*4*), New Zealand (*6*), Scotland (*5*), and Sweden (*9*). In contrast, transmission of the largely zoonotic *C. parvum* remained comparatively stable, as observed in New Zealand (*6*). A similar pattern appears to have occurred in Spain, where all *Cryptosporidium*-positive samples detected immediately after the pandemic were identified as *C. parvum*, with no evidence of *C. hominis* circulation in the investigated population (*7*).

The postpandemic resurgence observed in 2023 (Table 3), after interruption of *C. hominis* transmission

(*7*), was accompanied by an unprecedented increase in cryptosporidiosis cases across Europe (*10*,*11*). An additional contributing factor might have been an immunity debt effect resulting from reduced *Cryptosporidium* exposure during COVID-19 restrictions, particularly among children. In Spain, molecular data were initially limited to investigations of waterborne outbreaks in several regions (*11*), revealing a striking shift in subtype distribution. *C. hominis* accounted for 94.3% of genotyped samples; the rare subtype IfA12G1R5 was responsible for most (66.1%) infections. Because this subtype had been detected only sporadically before the pandemic (*12*), its predominance suggests either recent introduction or expansion from previously undetected low-level circulation. Our study expands those observations by providing baseline (nonoutbreak) epidemiologic data showing a similar predominance of *C. hominis* (96.0%), with IfA12G1R5 accounting for 67.5% of infections. The concordant patterns observed in both outbreak-related and sporadic cases indicate that expansion of IfA12G1R5 is not restricted to outbreaks but reflects sustained communitywide transmission in Spain.

IfA12G1R5 was recognized as a hypertransmissible lineage with a marked capacity for rapid spread, which could explain its predominance in the numerous outbreaks reported in Spain during the second half of 2023. In Europe, IfA12G1R5 was initially detected at low frequencies in the United Kingdom (*13*), as well as in Germany and Sweden (*14*) and Spain (*12*). Of note, IfA12G1R5 had already become the predominant *C. hominis* subtype in the United States (*15*) before the pandemic. Phylogenomic evidence indicates that IfA12G1R5 has multiple ancestral origins, involving introductions from East Africa and Europe followed by recombination events, which likely enhanced its fitness and transmission potential (*15*).

In contrast, the historically dominant IbA10G2 subtype declined sharply in 2023 (1.6%), indicating subtype replacement, consistent with molecular data from outbreak investigations conducted in Spain that year, which identified IbA10G2 in only 1 (0.8%) isolate (*11*). The shift might reflect a founder effect associated with reestablishment of transmission chains after the pandemic, favoring the expansion of a hypertransmissible subtype such as IfA12G1R5. Similar displacement of IbA10G2 by IfA12G1R5 or other *Cryptosporidium* subtypes has been documented in the United Kingdom (*10*) and the United States (*15*), although the underlying mechanisms and epidemiologic drivers remain unclear and appear unrelated to pandemic-associated disruptions.

C. parvum was detected only sporadically in 2023. The persistence of IIa subtypes at low frequency, together with absence of IIc and IId subtypes, suggests that zoonotic transmission did not undergo postpandemic amplification. That finding supports the hypothesis that nonpharmaceutical interventions selectively altered anthroponotic transmission pathways while largely sparing zoonotic cycles. However, differences in geographic coverage and sampling periods among datasets might have affected the observed patterns, influencing zoonotic transmission dynamics of *C. parvum*.

Our findings point to a dual epidemiologic scenario in which stable zoonotic transmission of *C. parvum* coexists with the rapid expansion of highly transmissible, human-adapted *C. hominis* subtypes such as IfA12G1R5. Clinicians in Spain should be aware of increases in infections caused by this emergent subtype.

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