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The role of endoscopic retrograde cholangiopancreatography in the treatment of hepatic cystic *Echinococcus* in a high HIV prevalence population: a retrospective cohort study

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Background: Endoscopic retrograde cholangiopancreatography (ERCP) is a useful, minimally invasive intervention in managing complicated hepatic cystic echinococcosis (HCE). This study aims to assess the use of ERCP in a South African HCE cohort with and without human immunodeficiency virus (HIV) co-infection.
Methods: An analysis was performed of patients with HCE who were assessed for surgery and underwent ERCP at a tertiary hospital in South Africa between 2011 and 2023. Demographics, clinical data, imaging characteristics, operative management, and postoperative complications were compared between HIV-negative (HIV-) and HIV-positive (HIV+) cohorts.
Results: Of the 91 patients assessed, 45 (mean age 34.6 years, 73.3% females, 23 HIV+) required ERCP. HIV status did not significantly affect cyst characteristics or surgical outcomes. HIV+ patients had a higher incidence of intraoperative bile leaks ($p = 0.025$). There were 18 patients who underwent preoperative ERCPs, mainly for biliary-cyst complications primarily causing obstructive jaundice. A total of 40 patients required postoperative ERCPs, mainly for bile leaks. There were no ERCP-related mortalities and only one case of pancreatitis. ERCP success rates were comparable in both cohorts, with an overall success rate of 86.7%.
Conclusion: HIV co-infection did not significantly impact the clinical course or outcomes of cystic echinococcosis (CE) patients undergoing ERCP. Perioperative ERCP proved effective in managing biliary complications of HCE as well as postoperative complications, regardless of HIV status. This study underscores the importance of endoscopic interventions in the comprehensive management of CE.
Keywords: hepatic cystic echinococcosis, HIV, endoscopic retrograde cholangiopancreatography

Introduction

CE is caused by the cestode *Echinococcus granulosus* (EG), which normally follows a sheep-dog host cycle but may accidentally infect humans who are dead-end hosts.[1-3] Incubatory cysts may lodge in various organs in the body, most notably the liver, causing HCE.[1-3] HCE has a long latency period, is frequently asymptomatic, and potentially self-limiting. However, in a third of patients, it may progress and become symptomatic or complicated with secondary infection or rupture into the peritoneal cavity or the biliary system.[2-5]

In countries with an overlap in geographical distribution of parasitic infestations and HIV, it has been speculated that the fast spread of HIV may be linked to increased susceptibility to HIV in patients with helminthic infestations.[6] Anecdotal conjecture is that the corollary is also true, that HIV in weakening the immune system increases the chances of a more severe parasitic burden.[6-8] Data on HCE treatment outcomes between HIV- compared to HIV+ patients are limited to small case series.[8-15] Despite this, based on the available data, it has been suggested that HIV-HCE co-infected patients present with a more complicated clinical course, including biliary obstruction, secondary infection, and cyst rupture, while having increased complication rates postoperatively.[8-12]

ERCP has evolved as an important minimally invasive intervention in managing the biliary complications of HCE and is performed pre-, intra- or postoperatively.[5,16,17] Indications for preoperative, and less commonly intraoperative, ERCP include mapping of the bile duct anatomy to demonstrate cyst-bile duct communication or for biliary drainage in patients with obstructive jaundice or cholangitis due to cystic material in the bile ducts.[5,16,17] Postoperative ERCP is used for treating postoperative complications, in particular, biliary leaks, which may occur in up to 63% of patients.[5,16,17]

The purpose of this study was to assess the use and outcomes of ERCP in a patient cohort with and without HIV co-infection treated for HCE in a tertiary referral hospital in South Africa.

Patients and methods

All patients who were assessed for surgery for HCE and in whom the HIV status was known in the Division of General Surgery at Groote Schuur Hospital (GSH) between 1 January 2011 and 30 September 2023 and required an ERCP as part of their management were included in the study. Data were collected from an ethically approved, prospectively maintained institutional registry. Demographic and clinical data, imaging characteristics as assessed on cross-sectional imaging, operative management, and postoperative complications were analysed for the total patient cohort and compared in HIV- and HIV+ patients. Similarly, ERCP data, including timing, indications, number of ERCPs per patient, findings at ERCP, and interventions performed, were analysed in the total cohort and compared in HIV- and HIV+ patients. All imaging, including ERCP images, was analysed by two blinded radiologists. The senior author resolved differences in assessments.

Statistical analysis

Registry data were recorded in REDCap (Research Electronic Data Capture).[18,19] All tables were analysed using SPSS (Statistical Package for the Social Sciences) version 26.[20] Pearson's chi-square test was used to assess the variance between different categories, ensuring that all test assumptions were adequately met. In some categories, due to insufficient sample size that did not meet the chi-square test assumptions, Fisher's exact test was implemented instead, and corresponding *p*-values were calculated. For continuous variables and independent samples, the t-test was used to assess variance among the means. A threshold for statistical significance of $p < 0.05$ was used.

Results

Of the 91 patients with HCE assessed for surgery, 87 underwent an operation. A total of 45 patients underwent one or more ERCP examinations and comprised the study cohort. Of these, 44 patients underwent an operation. One patient who underwent ERCP biliary stenting was treated with antibiotics and percutaneous drainage for an infected cyst with complete cyst resolution and did not undergo surgery. The mean age of patients in the ERCP cohort was 34.6 years, and 33 (73.3%) were female (Table I). Of the patients, 22 (48.9%) were HIV+, of whom 70% had advanced HIV. Also, 32 (71.1%) patients, 16 in each group, presented with complicated disease, defined as obstructive jaundice ($n = 19$, 42.2%), cholangitis ($n = 15$, 33.3%), secondary cyst infection ($n = 14$, 31.1%), cyst rupture ($n = 12$, 26.7%), or anaphylaxis ($n = 1$, 2.2%).

Laboratory parameters were similar in the two groups, except for total bilirubin levels, which were higher in the HIV- group, with 66.78 µmol/L versus 22.36 µmol/L in the HIV+ group ($p = 0.016$). There were no differences in the cyst characteristics, extent of disease, or liver imaging findings in the HIV- and HIV+ groups on cross-sectional imaging (Table II).

The two groups had no differences in the number of preoperative or postoperative ERCPs per patient. Preoperative ERCP was performed in 18 (19.8%) of the 91 patients assessed for surgery. The predominant indication for preoperative ERCP, obstructive jaundice, was present in 15 (83.3%) patients, of whom nine had associated cholangitis (Table III). Significantly, eight (72.7%) HIV- patients were found to have bile duct dilation on ERCP, compared to a single HIV+ patient ($p = 0.016$). Other findings included similar numbers of patients with intraluminal cysts and biliary-cyst communication. However, in one HIV+ patient, biliary-cyst communication was complicated by the

Table I. Demographic, clinical presentation data for the ERCP patient cohort in HIV negative and positive patients.

	Total		HIV negative		HIV positive		*p*-value
	n	**%**	***n***	**%**	***n***	**%**	
Patients	45	100	23	51.1	22	48.9	0.833
	Mean	SD	Mean	SD	Mean	SD	
Age	34.6	±11.34	35.6	±14.36	33.5	±7.14	0.270**
Gender	***n***	**%**	***n***	**%**	***n***	**%**	
Female	33	73.3	17	73.9	16	72.7	0.928
Male	12	26.7	6	26.1	6	27.3	0.928
Medical history							
Comorbidities	16	35.6	5	21.7	11	50	0.477
Uncomplicated	13	28.9	7	30.4	6	27.3	0.815
Complicated[§]	32	71.1	16	69.6	16	72.7	0.815
Anaphylaxis	1	2.2	1	4.3	0	0.0	1*
Obstructive Jaundice	19	42.2	12	52.2	7	31.8	0.167
Cholangitis	15	33.3	11	47.8	4	18.2	0.035
Grade 1	4	8.9	3	13.0	1	4.5	0.317
Grade 2	11	24.4	8	34.8	3	13.6	0.099
Secondary cyst infection	14	31.1	10	43.5	4	18.2	0.067
Cyst rupture	12	26.7	7	30.4	5	22.7	0.559

[§] Patient assigned diagnosis based on clinical findings, laboratory results and imaging
* Fischer exact test was performed
** Independent samples T-test was performed

Table II. Imaging characteristics of the ERCP cohort in HIV negative and positive patients on cross-sectional imaging.

	Total		HIV negative		HIV positive		*p*-value
	n	%	*n*	%	*n*	%	
Patients	45	100	23	51.1	22	48.9	0.833
	Mean	SD	Mean	SD	Mean	SD	
Diameter of largest cyst	13.4	±4.71	12.2	±4.64	14.7	±4.51	0.109**
Cyst number	*n*	%	*n*	%	*n*	%	
Single	25	55.6	14	60.9	11	50.0	0.463
Multiple	20	44.4	9	39.1	11	50.0	0.463
Affected segment							
Segment 1	6	13.3	5	21.7	1	4.5	0.090
Segment 2	13	28.9	8	34.8	5	22.7	0.372
Segment 3	10	22.2	5	21.7	5	22.7	0.936
Segment 4	28	62.2	17	73.9	11	50.0	0.098
Segment 5	25	55.6	11	47.8	14	63.6	0.286
Segment 6	24	53.3	10	43.5	14	63.6	0.175
Segment 7	30	66.7	13	56.5	17	77.3	0.140
Segment 8	29	64.4	14	60.9	15	68.2	0.608
Bile duct dilation	10	22.2	7	30.4	3	13.6	0.175
Bile duct/cyst communication	8	17.8	5	21.7	3	13.6	0.477
Intra-biliary cysts	4	8.9	3	13.0	1	4.5	0.317
Cyst calcification	3	6.7	2	8.7	1	4.5	0.577

** Independent samples T test was performed

Table III. Indications, findings and interventions in HIV negative and positive patients whom required pre-operative ERCP.

	Total		HIV negative		HIV positive		*p*-value
Pre-operative ERCP	18		11		7		
	n	%	*n*	%	*n*	%	
Indication							
Mapping of biliary anatomy	2	11.1	0	0	2	28.6	0.137*
Obstructive jaundice	15	83.3	10	90.9	5	71.4	0.280
Cholangitis	9	50	7	63.6	2	28.6	0.147
Findings							
Bile duct dilatation	9	50	8	72.7	1	14.3	0.016
Biliary-cyst communication	11	61.1	7	63.6	4	57.1	0.783
Intra-luminal cysts	7	38.9	5	45.5	2	28.6	0.474
Intervention							
Sphincterotomy	15	83.3	9	81.8	6	85.7	0.829
Biliary stenting	14	77.8	8	72.7	6	85.7	0.518
Clearance of cystic material	7	38.9	5	45.5	2	28.6	0.474

* Fischer exact test was performed

complete destruction of the hepatic confluence (Figure 1). There were no differences between the groups in preoperative ERCP interventions, with most undergoing sphincterotomy (83.3%) and/or biliary stenting (77.8%).

Pericystectomy was the most frequently performed operation in the total surgical group. In the ERCP cohort, pericystectomy was performed in 18 (78.3%) HIV- and 20 (95.2%) HIV+ patients, while anatomical liver resection was performed in five (21.7%) HIV- patients and none of the HIV+ patients ($p = 0.049$). Significantly, intraoperative bile leaks were found in 15 (68.2%) of HIV+ patients but only in eight (34.8 %) of the HIV- group ($p = 0.025$). Of the 87 operated patients, three (3.4%) had an intraoperative ERCP, and 51 (58.6%) had one or more surgical complications (76.5% Accordion grade 1–3), of whom 40 (46.0%) required one or more postoperative ERCP.[21]

Bile leak was the most common surgical complication in the ERCP cohort, present in 31 (70.5%) of the 44 operated patients, 30 of whom required an ERCP with actual bile leaks demonstrated in 29 patients with no differences observed between the two groups (Table IV). Most leaks (79.2%) were low-grade, and the majority (76.0%) were from the right liver. Biliary stenting was performed in 25 patients, and sphincterotomy without stenting in four. In one patient, residual cystic material was removed from the bile ducts. Nine ERCPs were performed only to remove stents

Table IV. Indications, findings and interventions in HIV negative and positive patients who required post-operative ERCP.

	Total		HIV negative		HIV positive		*p*-value
Post-operative ERCP	40		20		20		
	n	%	*n*	%	*n*	%	
Indication							
Suspected bile leak	31	77.5	14	70.0	17	85.0	0.256
Removal of intra-luminal cysts	1	2.5	0	0.0	1	5.0	1*
Diagnostic	2	5.0	0	0.0	2	10.0	0.487*
Removal of stent only	9	22.5	6	30.0	3	15	0.256
Findings							
Bile leak demonstrated	29	72.5	13	65.0	16	80.0	0.288
Intervention							
Biliary stenting	25	62.5	13	65.0	12	60	0.744
Sphincterotomy	4	10.0	1	5.0	3	15.0	0.605*
Clearance of cystic material	1	2.5	0	0.0	1	5.0	1*
Bile leak site appraisable (*n*)	(25)		(10)		(15)		
Left liver	6	24.0	2	20.0	4	26.7	0.702
Right liver	19	76.0	8	80.0	11	73.3	0.702
Grade of bile leak quantifiable (*n*)	(24)		(9)		(15)		
High	5	20.8	2	22.2	3	20.0	0.897
Low	19	79.2	7	77.8	12	80.0	0.897
Number of stents placed (*n*)	(25)		(13)		(12)		
1	23	92.0	12	92.3	11	91.7	0.953
2	2	8.0	1	7.7	1	8.3	0.953

* Fischer exact test was performed

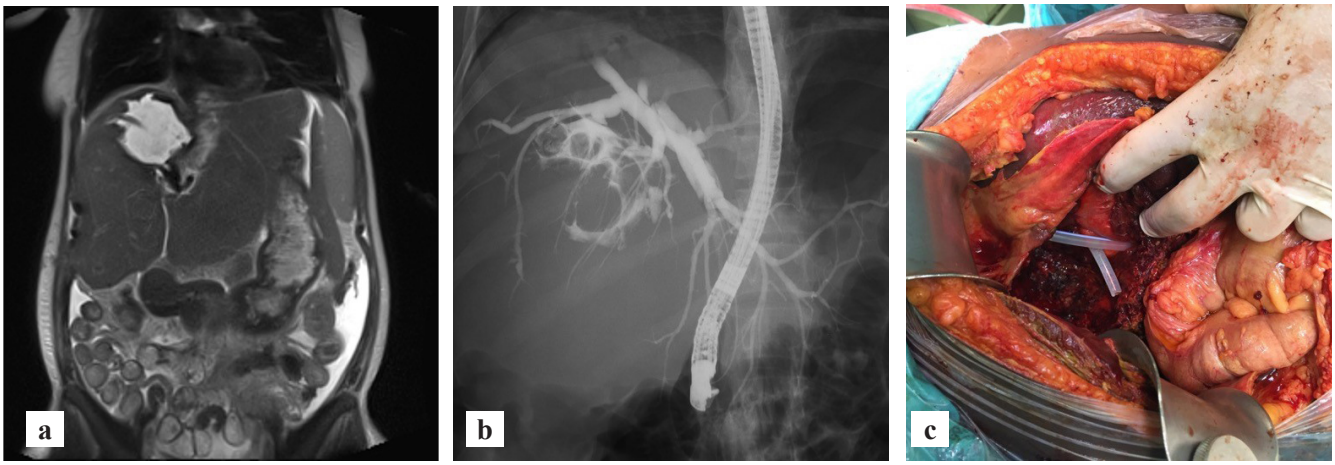

Figure 1. A 38-year old HIV positive female presented with obstructive jaundice and weight loss. a) An MRI/MRCP showed a 6 cm central hepatic cyst with marked atrophy of the right liver and hypertrophy of the left liver, b) ERCP clearly demonstrated a contrast leak from the hilar area with filling of only the left-sided ducts and extravasation into a right-sided cyst with no filling of bile ducts on the right, c) at surgery there was complete destruction of the hilum with only openings to the common hepatic and left hepatic ducts visible.

placed before or during surgery, and two patients did not need endoscopic intervention.

There were no ERCP-related mortalities and only one post-ERCP complication (an HIV+ patient who developed mild pancreatitis). The mean hospitalisation for the ERCP cohort was 19.65 days compared to 10.35 days for patients not undergoing an ERCP. The cumulative ERCP treatment outcome was successful in most patients (86.7%), with ERCP treatment deemed unsuccessful in only three patients in each group.

Discussion

This study evaluated the role of perioperative ERCP in patients who underwent surgery for HCE, comparing patients with and without HIV co-infection. Reliable data on CE prevalence in South Africa is lacking, but it is estimated to be 11% in the Eastern Cape province, from where most patients managed at our institution are referred.[8,22] The same province has reported one of the highest HIV prevalences in South Africa, with 36.5% of antenatal females testing positive for HIV.[23] The prevalence of HIV co-infection

in the ERCP cohort (48.9%) exceeds the national HIV prevalence of roughly 13% in South Africa.[8,24] The female predominance in this study (73.3%) is consistent with results published from sub-Saharan African and Mediterranean countries.[9,22] However, previous studies focusing only on HCE patients who required endoscopic interventions reported a more equal gender distribution, which has led to hypotheses that male patients may be more prone to biliary complications.[16,17,25] The mean age of our ERCP cohort was 34.6 years, slightly younger than reported ERCP cohorts in patients without HIV of between 36.3 and 46.5 years.[16,17,26]

More than two-thirds of the 91 patients who were assessed for surgery presented with complicated disease, defined as obstructive jaundice with or without cholangitis, secondary cyst infection and cyst rupture, and required urgent treatment. The literature reports that while approximately 60% of all CE patients remain asymptomatic, 30–60% of HCE patients develop complications.[25] Biliary-cyst communication is the most frequent preoperative complication of HCE, occurring in up to 42% of patients who may be asymptomatic or present with jaundice, cholecystitis, cholangitis, liver abscess, pancreatitis, or septicaemia.[5,17,25]

Cyst infections, an indicator of biliary-cyst communication, previously reported in approximately 20% of patients, were present in 31.1% of patients in our ERCP cohort.[5,25] Potential risk factors for biliary-cyst communication include advanced patient age, male gender, and multiple, centrally or caudate-located, calcified or large cysts (with a cut-off of 7.5–14 cm).[5,25-27] The mean diameter of the largest cysts in patients in our cohort was 13.4 cm, which would have put a minimum of 50% of patients at a higher risk due to cyst size. Preoperative ERCPs were required in 20% of patients who were assessed for surgery, with the predominant indication being obstructive jaundice. Similar numbers were reported in previously published studies.[5,16,17,28]

Complications related to biliary-cyst communication also remain a concern after surgery for HCE. ERCP may identify major biliary-cyst communications (defined as > 5 mm, reported to occur in 3–17% of HCE patients) in most patients (86–100%), but it has a lower sensitivity in detecting minor communications with false negatives reported in as many as 20% of patients.[17,25,29,30] Minor communications between the cyst and small biliary radicals, present in 10–37% of HCE patients, are often asymptomatic, difficult to demonstrate pre- and intraoperatively, and more often present as postoperative bile leaks.[5,27]

The surgical complication rate of 58.6% in the 87 operated patients is higher than the 5.5–50% reported in previous studies in patient cohorts with no concomitant HIV infection.[5,21,25-27,29] In our study, no differences in the incidence or severity of complications between the HIV- and HIV+ patients were observed. The higher complication rates in our patients are more likely related to the high percentage of patients who presented with advanced and complicated diseases. Of all operated patients, 40 (46.0%) required one or more postoperative ERCPs, of which 31 were for bile leaks. A bile leak was demonstrated in 29 (33.3%) patients, which conforms with reported bile leak rates (22–63%) in the literature.[5,17,28,30] In line with previous studies, most leaks were from the right-sided biliary tree.[5]

Our study's overall ERCP success rate of 86.7% aligns with previous findings.[5,17] Success rates of 80–100% for preoperative ERCPs and > 90% for postoperative ERCPs have been reported alongside low mortality and morbidity rates.[5,16,17] We had no ERCP-related mortalities and only one post-ERCP complication.

Limited research suggests that CE is more severe with concomitant HIV, although the exact mechanism remains uncertain.[8-12] One hypothesis suggests that untreated HIV suppresses the host immune defence against parasites by shifting to a Th2-dominant immune response, potentially resulting in increased disease acquisition, faster progression, and more complications in patients with HCE.[6,8,10] This hypothesis is not supported by the findings of this study, with the only significant difference between HIV- and HIV+ patients being the incidence of intraoperative bile leaks that were present in 70% of HIV+ patients compared to 35% of HIV- patients.

A limitation of this study is the retrospective data analysis in a consecutive patient cohort rather than in a matched format. The primary strength of the study is the use of real-life data, which makes results representative of standard practice. Furthermore, this is the first known study to compare the use and outcomes of perioperative ERCP in HCE patients with and without HIV co-infection.

Conclusion

In conclusion, approximately half of our study's HCE patients assessed for surgery required an endoscopic intervention. The prevalence of HIV in our study, which exceeds the national HIV prevalence, may suggest that HIV co-infection predisposes HCE patients to more complicated diseases. However, patients in our study presented with equivalent levels of disease severity and HCE complications regardless of HIV status. Although the rate of postoperative complications was higher than previously reported, no apparent differences were observed between HIV- and HIV+ patients.[5,25-27,29] The use of perioperative ERCP was similar in the two groups and equally effective in treating the biliary complications of HCE.

Conflict of interest

The authors declare no conflict of interest and affirm that the submitted manuscript is their original work and is not under consideration by another journal.

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Ethical approval

The Human Research Ethics Committee (HREC), Faculty of Health, University of Cape Town, approved the HHD registry (HREC/REF: R019/2016) and this study (HREC/REF: R787/2023).

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