

Amoebiasis in Pregnancy: A Review and Update of the Literature

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Abstract

Amoebiasis is a disease which tends to be caused mainly by *Entamoeba histolytica*. Amoebiasis can affect males, females, children, and adults. Amoebiasis tends to be more commonly encountered in people who live in or travel to developing countries that are amoebiasis endemic area with poor sanitary conditions. Individuals from the developed countries who travel to and back from developing countries or individuals in developed countries who have not travelled to developing countries but have been close to their relatives or friends who have travelled to developing countries could also develop amoebiasis. Individuals who are infected by amoebiasis are not always symptomatic as well as some individuals who have been harbouring *entamoeba histolytica* may be asymptomatic for many years before they become symptomatic which makes it difficult for the patients and their clinicians to have a high index of suspicion for the possibility of amoebiasis which would contribute to mis-diagnosis or delay in the diagnosis that would tend to be associated with the possible development of complications including amoebic liver abscess and perforation of the abscess with the development of peritonitis when the diagnosis is not established quickly. Amoebiasis could be asymptomatic or it could be associated with mild or severe symptoms. Some of the common symptoms of amoebiasis include lethargy, weight less, abdominal pain, diarrhoea, bloody diarrhoea. Some of the complications of amoebiasis include inflammation as well as perforation with tissue of the colon or peritonitis. Extra-intestinal amoebiasis may also develop leading to amoebiasis of the liver and amoebic liver abscess, amoebic pneumonitis, amoebic infections of the brain and cerebral abscess, amoebic vaginitis, amoebic cervicitis, amoebic endometritis, amoebic salpingitis, amoebiasis of the ovary with or without the development of an abscess, amoebic prostatitis, amoebiasis of the kidney and amoebic emphysematous pyelonephritis and amoebic renal cyst, amoebiasis mimicking fibroid, amoebic peri-carditis, and amoebic cardiac tamponade. Some of the predisposing factors for the development of amoebiasis include: exposure to amoebiasis infected individuals, drinking of unsafe water, alcoholism, ages extremes including the elderly and young children, pregnancy, immunosuppression, recent coital activity with unprotected anal or oral-anal contact, recent travel to developing countries and residence within an amoebiasis endemic developing country or region. Amoebiasis may mimic appendicitis, Crohn's disease, ulcerative colitis, colonic malignancy and other more common conditions. Globally about 50 million cases of invasive *Entamoeba histolytica* infection occurs per year leading to as many as many as 100,000 deaths that is believed to be the tip of an iceberg. A high index of suspicion is required to establish quickly a diagnosis of amoebiasis generally as well as amoebiasis in pregnancy. Diagnosis of enteric amoebiasis whether associated with pregnancy in medical establishments in rural hospitals in the developing countries has tended to be based upon microscopy examination of stool samples of patients. Nevertheless, molecular -biology based tests with serology tests by polymerase chain reaction (PCR) tests tend to provide a quick and accurate diagnosis but these tests tend not to be immediately available in small hospitals of some developing countries. In complicated cases like amoebic liver abscess microscopy examination of the abscess fluid aspirate and biopsy of the wall of the abscess would tend to confirm the diagnosis. Few epidemiological data relating to the prevalence of *Entamoeba histolytica* within Europe and North America do exist; nevertheless, studies that had investigated infectious travel-related gastrointestinal disorders had reported that amoebiasis is the identified pathogen in 1.4% of cases in Europe. Considering that both within the developing countries and developed countries Amoebiasis in pregnancy is not excessively common, without a high index of suspicion for the possibility of a pregnant woman who presents with non-specific symptoms as stated above there would tend to be a delay in the diagnosis of amoebiasis in stool microscopy, PCR studies and ultrasound scan of abdomen and pelvis is not undertaken quickly. If stool microscopy, PCR studies, and quick aspiration and biopsies and pathology examinations of specimens of amoebic liver abscesses / lesions associated with pregnancy are undertaken then a diagnosis of amoebiasis in pregnancy would be made and a quick and appropriate treatment would be provided. Or else complications of amoebiasis including perforation of bowel, perforation of amoebic liver abscess/ amoebic liver abscess related atelectasis and chest infection would develop which would tend to be associated with prolonged morbidity and at times mortality. Treatment of amoebiasis associated with pregnancy entails utilization of anti-amoebic medications (for example metronidazole), treatment of any concurrent bacterial infection with an appropriate antibiotics, supportive care, and treatment of complications including amoebic liver abscess by

radiology image-guided (ultrasound scan or magnetic resonance imaging scan) aspiration and drainage of the abscess or at times laparotomy. Regular follow-up clinical and radiology imaging follow-up assessment of patients is important to ascertain there is no recurrence of an abscess and education related to sanitary dietary habits is important to prevent further development of amoebiasis.

Key Words: amoebiasis; pregnancy; entamoeba histolytica; entamoeba dispar; Microscopy; stool; bloody diarrhea; liver abscess; PCR; ultrasound scan; magnetic resonance imaging scan; metronidazole; antibiotics; supportive care; aspiration; drainage; laparotomy; biopsy; colon; trophozoites

Introduction

It has been iterated that globally about 50 million cases of invasive *Entamoeba histolytica* disease tends to occur every year which does tend to emanate in as many as 100,000 deaths. [1] It has also been iterated that the documented incidence and death rates attributable to amoebiasis globally do represent the tip of an iceberg in view of the fact that only 10% to 20% of individuals who are infected by amoebiasis tend to be symptomatic [1-3]. It has also been stated that the incidence of amoebiasis is higher within the developing countries. [1, 5]. It has also been iterated that amoebiasis is the second leading cause of death attributable to parasitic diseases and this does kill 40,000 to 100,000 individuals globally each year [1] [6] It has been iterated that the earlier estimates of *Entamoeba histolytica* which had been based upon examination of stool for ova, parasites, have tended not to be accurate, in view of the fact that the test cannot be used to differentiate *Entamoeba histolytica* from *Entamoeba dispar* and *Entamoeba Moshkovskii* within developing nations, and the prevalence of *Entamoeba histolytica* which has been determined based upon enzyme-linked immunosorbent assay (ELISA) or polymerase chain reaction (PCR) assay of stool from asymptomatic individuals had ranged from 1% to 21% [1]. It has been iterated that upon the basis of current techniques of testing for amoebiasis, it has been estimated that 500 million individuals who have *Entamoeba* infection tend to be colonized by *Entamoeba dispar* [1, 7]. It has been documented that the prevalence of *Entamoeba* infection is as high as 50% within areas of Central America, Africa, as well as Asia [1, 8]. It has been iterated that studies on seroprevalence of *Entamoeba histolytica* within Mexico showed that 8% of the population were positive for *Entamoeba histolytica* [1, 9]. It had also been iterated that within amoebiasis endemic areas of the world, as many as 25% of patients could be carrying antibodies to *Entamoeba histolytica* as a result of their previous amoebiasis infection, which could be largely asymptomatic. [1] it had additionally been iterated that the prevalence of asymptomatic *Entamoeba histolytica* infections does appear to be dependent upon the region of the world in that within Brazil for example, the incidence of *Entamoeba histolytica* infection could be as high as 11% and within Egypt, 38% of patients who manifest with acute diarrhoea to an outpatient clinic were found to have amoebic colitis [1, 6]. It has been documented that a study that was undertaken within Bangladesh had revealed that pre-school children had experienced 0.09 episodes *Entamoeba histolytica* associated diarrhoea as well as 0.03 episodes of amoebic dysentery every year [1]. It has been documented that within the city of Hue in Vietnam, the yearly incidence of amoebic liver abscess had been reported to be 21 cases per 100,000 inhabitants [1, 10]. Despite the various documentations related to the incidence of amoebiasis globally, amoebiasis associated with pregnancy has only been reported sporadically and some of the cases had been misdiagnosed initially or there had been delay in the diagnosis of the disease for various reasons including the non-specificity of the symptoms and the fact that within the developed countries where amoebiasis tends to be rarely encountered clinicians would tend not to have a high index of suspicion for the infection even in patients who have travelled to amoebiasis endemic area as well as it is even more difficult to suspect amoebiasis in a pregnant lady who has never travelled outside the developed countries. Amoebiasis can affect males and females, children and adults. Pregnant ladies can also develop amoebiasis. Nevertheless, considering the fact

that globally very few pregnant ladies tend to develop amoebiasis, the diagnosis of amoebiasis could be delayed or mis-diagnosed and by the time the correct diagnosis complications could have occurred and this would tend to lead to morbidity and at times mortality of the patients. In view of this it is important for all clinicians globally to know about the manifesting features of amoebiasis pregnancy to be known in the developed countries where amoebiasis tends to be encountered occasionally as well as in developing countries where amoebiasis is common but uncommonly encountered in pregnant ladies so that complications of amoebiasis and death can be avoided and early correct treatment can be provided to ameliorate the lives of pregnant women who develop amoebiasis. . Extra-intestinal can affect various organs of the body including the liver, lungs, brain, genital organs. The ensuing article on amoebiasis associated with pregnancy is divided into two parts: (A) Overview which has discussed general aspects of amoebiasis and (B) Miscellaneous narrations and discussions from some case reports, case series and studies related to amoebiasis associated with pregnancy.

Aims

To review and update the literature on amoebiasis in pregnancy.

Methods

Internet data bases were searched including: Google, Google Scholar, Yahoo, and PUBMED. The search words that were used included: Amebiasis in pregnancy; Amoebiasis in pregnancy; Pregnancy associated amoebiasis; Pregnancy associated amebiasis. Amoebiasis. Amebiasis. Fifty three references were identified which were used to write the article which has been divided into two parts: (A) Overview which has discussed general aspects of amoebiasis and (B) Miscellaneous narrations and discussions from some case reports, case series, and some studies related to amoebiasis in pregnancy.

Results / Review and Update of Literature on Amoebiasis in Pregnancy

(A) Overview

Definition / general statements

- Amoebiasis is a terminology that is utilized for an infection which is caused by pathogenic species of amoebae, and most commonly has tended to be caused by *Entamoeba histolytica* [11].
- It has been stated that amoebiasis could be present with no, mild, or symptoms [12, 13].
- It has been iterated that generally the symptoms of amoebiasis could include: lethargy, weight loss, colonic ulcerations, abdominal pain, diarrhoea, or bloody diarrhoea [12-14].
- It has been stated that some of the complications of amoebiasis do include inflammation and ulceration of the colon with the development of tissue death or perforation of the bowel which might emanate in the development of peritonitis [12].

- It has additionally been iterated that individuals who are affected by amoebiasis could develop anaemia in view of prolonged gastric bleeding [12, 13].
 - Amoebiasis may affect males, females, children and adults.
 - Even though amoebiasis in pregnancy tends to be uncommonly encountered, it is important for clinicians to be aware that amoebiasis could also affect pregnant ladies therefore a high index of suspicion would be required to establish the diagnosis of amoebiasis in pregnancy.
 - It has been iterated that the diagnosis of amoebiasis generally tends to be undertaken by examination of the stool with utilization of the microscope; nevertheless, stool examination may not reliably exclude infection or separate specific types of amoebiasis. [12, 13].
 - It has additionally been stated that an increased white blood cell count could be present in severe cases of amoebiasis [12, 13].
 - It has furthermore been iterated that the most accurate test with regard to the diagnosis of amoebiasis is the finding of specific antibodies within the blood; nevertheless, the antibodies may remain positive pursuant to treatment [12, 13].
 - It has also been stated that bacterial colitis could simulate amoebiasis [12, 13].
 - It has been iterated that amoebiasis, which is caused by infection with the anaerobic protozoan *Entamoeba histolytica* and other *Entamoeba* species [12, 15], had been recognized as the fourth-leading cause of death by parasite infection globally [12, 15, 16].
 - It has also been stated that yearly, about 50 million patients do develop symptoms of amoebic dysentery or extra-intestinal disease with an estimated 50,000 to 100,000 deaths per year which has been caused by complicated infection of this unique pathogen [6, 15-20].
 - It has been iterated that with humans and perhaps human-like primates as the only natural hosts of amoeba, the sources of infection have tended to be water that has been contaminated with *Entamoeba* cysts or on more rare occasions via faecal-oral contacts [6, 12, 15, 21].
 - It has been stated that majority of developing countries that have poor sanitation standards tend to be endemic countries for amoebiasis, while most cases of amoebiasis within the developed countries of the Western world do tend to arise from immigration and patients traveling to and back from endemic areas. It has additionally been iterated that the prevalence of amoebiasis tends to be higher in young men in comparison with women, and amoebiasis also tends to be common in patients who are on immunosuppressants as well as in HIV-positive patients [6, 12, 15, 17, 18].
 - It has been pointed out that pregnancy is a known risk factor for development of invasive amoebiasis
 - It has additionally been iterated that few epidemiological data relating to the prevalence of *Entamoeba histolytica* within Europe and North America do exist; nevertheless, studies that had investigated infectious travel-related gastrointestinal disorders had reported that amoebiasis had been the identified pathogen in 1.4% of cases within Europe [12, 15, 24].
 - It has been stated that with regard to the majority of cases of amoebiasis which amount to greater than 90% of cases of amoebiasis, infection with *Entamoeba* species, especially the non-pathogenic commensal *Entamoeba dispar*, has tended to be asymptomatic or self-limiting [6, 12, 15].
 - Nevertheless, about 10% of patients do develop invasive amoebiasis, and majority of these patients tend to suffer from amoebic dysentery or amoebic colitis. Within a period of approximately 8 weeks to 20 (median 12 weeks) pursuant to exposure, patients do tend to report the subacute onset of the typical symptoms of amoebiasis that include abdominal pain, fever and diarrhoea with bloody and mucous stools [12, 15, 18].
 - It has been documented that One out of 10 patients who have invasive amoebiasis would develop extra-intestinal disease, with amoebic liver abscesses (ALA) being the commonest form of the infection; these patients characteristically tend to manifest with increasing abdominal pain and tenderness within the right upper quadrant of the abdomen as well as fever over the course of a few days [6, 12, 15, 17, 25].
 - It has additionally been stated that apart from ALA, reports of cardiac, pleuropulmonary, cerebral as well as urogenital and dermatological complications secondary to amoebiasis have been documented [12, 15, 26-29].
 - It has been advised that with regard to the case of a suspected amoebic dysentery, direct microscopy of stool samples should be undertaken in order to identify the active form of *Entamoeba* species, the so-called trophozoite. [12, 15].
 - It has been iterated that within the developed countries, serological testing including ELISA, immunofluorescence testing do represent the standard of care for securing the correct diagnosis of amoebiasis. [12, 15, 30].
 - It has furthermore been stated that the diagnosis of amoebic liver abscess usually tends to be supported by radiology imaging studies which usually has tended to be the undertaking of ultrasound scan of the abdomen, contrast-enhanced ultrasound (CEUS) in centres where CEUS is available and high-resolution computed tomography in order to ascertain the local extent of the disease as well as infection-associated complications [12, 15, 30].
- Apart from the aforementioned radiology imaging studies, it would be argued ultrasound scan and contrast-enhanced ultrasound scan should be undertaken in the case of a suspected amoebic liver abscess in a pregnant lady but because of the radiation involved in computed tomography (CT) scan, computed tomography (CT) scan of abdomen and pelvis should not be undertaken in pregnant women who are suspected to have amoebic liver abscess; nevertheless. Magnetic resonance imaging (MRI) scan of the abdomen and pelvis could be undertaken.

Terminology

- It has been iterated that amoebiasis does also tend to be referred to as amebiasis [11]

Epidemiology [11]

- It has been stated that it has been estimated that 10% of the world's population is infected with *Entamoeba histolytica*

- Has been documented that *Entamoeba histolytica* is endemic within tropical and subtropical regions
- It has also been iterated that within temperate developed countries patients who have amoebiasis infection usually are immigrants, travellers, men who have sex with men, and residents of institutions
- It has been documented that other sources have stated that many, if not majority of, individuals who are believed to carry *Entamoeba histolytica* could be carrying non-pathogenic *Entamoeba. Dispar* or *Entamoeba. Moshkovskii* which are morphologically identical to *E. histolytica*
- It has been iterated that it has been estimated that there are fifty million cases of amoebic diarrhoea globally annually with 100,000 deaths

Sites [11]

- It has been iterated that amoebiasis does involve the colon, most commonly the cecum, followed by the ascending colon, the rectum, the sigmoid colon and the appendix
- It has also been iterated that involvement of the terminal ileum by amoebiasis could occur
- It has been stated that metastasis of amoebiasis or extra-intestinal amoebiasis could develop and overwhelmingly this does spread to the liver
- It has additionally been stated that amoebiasis could spread from the liver to the thorax or on rare occasions to the brain
- It has furthermore been iterated that rectovesical fistula and fistulous involvement of the skin as an emanation of amoebiasis had been reported

Pathophysiology [11]

The pathophysiology of amoebiasis has been summated as follows: [11]

- The amoeba cysts are ingested from food or from water which has been contaminated with faeces; and sexual transmission also does occur.
- Excystation to 8 motile trophozoites does occur within the small intestine
- The cysts are known to be resistant to gastric acid (and chlorine within water supplies)
- The amoeba trophozoites tend to be potentially invasive and they multiply by binary fission
- It has been documented that in an estimated 20% of amoebic infections invasion into the wall of the colon with tissue destruction does occur.
- It has been iterated that adherence of amoeba to colonic mucosa is mediated by a lectin upon the surface of *Entamoeba histolytica*
- It has been stated that the parasite then does induce apoptosis of epithelial cells through a channel forming pore protein
- It has been iterated that *Entamoeba histolytica* does ingest the remnant cells

- It has also been documented that some of the trophozoites do undergo encystation through signalling pathways that complete the cycle

Clinical features [11]

- The majority of individuals who have amoeba infection tend to be asymptomatic, but they do pass cysts and this tends to be referred to as asymptomatic intraluminal amebiasis [11].
- The aforementioned statement is said to be true for all cases of *Entamoeba. moshkovskii* and most of *Entamoeba. dispar* and up to 80% of *Entamoeba histolytica* infections
- It has been iterated that whilst *Entamoeba. dispar* is generally understood to be non-pathogenic, recent reports had indicated that it may sometimes cause symptoms [31].
- It has been documented that the commonest symptom from amebiasis has tended to be diarrhoea without dysentery meaning that there tends to be no mucus or blood within the stool
- Amoebic dysentery or colitis tends to manifest with mucus or grossly visible blood or non-visible blood which is found upon microscopic examination of the stool
 - 15% to 33% of cases of amoebic dysentery tend to manifest with diarrhoea
 - Usually symptoms in amoebic dysentery tend to develop gradually over three weeks to a month with worsening diarrhoea and abdominal pain
 - Symptoms of amoebic dysentery could also develop acutely and these cases could simulate acute abdomen
 - Cases of amoebic dysentery in which the symptoms develop months after infection could occur
 - Young children who develop amoebic dysentery could develop intussusception or necrotizing colitis which could be ensued by the development of perforation
 - Rare complications of amoebic dysentery do include toxic megacolon and / or colonic amebomas
 - Amoebic liver abscesses tend to be more commonly encountered in men in comparison with females with a male to female ration of 10:1.
 - The amoebic abscess usually tends to be solitary
 - Symptoms of the disease in some cases of amoebiasis tend to include fever, cough, and dull, achy right upper quadrant abdominal pain which could also include referred pain in the right chest or shoulder
 - It has been stated that only one out of three (1/3) patients who have amoebic liver abscess tend to manifest with gastrointestinal symptoms
 - It has been documented that the symptoms of amoebiasis usually tend to develop over a period of two to four weeks
 - The liver usually tends to be enlarged and tender

- Leucocytosis and elevated liver enzymes tend to be found in routine haematology and biochemistry blood test results.

Clinical examination:

- The general and systematic examination of many pregnant women who have amoebiasis may be normal and there may not be any abnormality on abdominal examination when they initially present.
- In cases of pregnant ladies who have amoebiasis with colonic involvement and who have bloody diarrhoea, rectal examination would tend to be normal but there could be visible blood within the stool that is found on the gloves of the examination figure.
- If a pregnant lady has amoebiasis of the vagina or amoebiasis of the cervix, there could be blood on the gloves of the examining finger upon vaginal examination but these are rare conditions. Additionally if there is amoebiasis of the endometrium there could be visible blood on the gloves of the examining finger.
- If a pregnant lady has amoebiasis of the liver plus liver abscess, there would tend to be tenderness in the right upper quadrant of her abdomen and at times the liver may be palpated to be enlarged or there could be dullness to percussion in the right upper quadrant of the abdomen of the patient.
- In cases of amoebiasis of the liver with liver abscess in a pregnant lady there may be decreased breath sounds within the lower basal area of her chest on the right.
- In the scenario of on-going amoebiasis and amoebic dysentery in a pregnant lady who has fever, diarrhoea, and inability to drink and eat well, there may be fever, evidence of dehydration, tachycardia, evidence of weight loss, or no weight gain over a period of a few weeks and at times evidence of intra-uterine growth retardation. There could be signs of tender in the abdomen which might simulate appendicitis, or ulcerative colitis or peritonitis.
- In cases of amoebic vaginitis or amoebic cervicitis inspection of the vagina and cervix area may show ulceration / inflammation that may simulate carcinoma of the ulcer or cervix and specimens of swabs and biopsies obtained from the vagina / cervix upon microbiology / pathology examination would confirm amoebiasis.

Investigations

Stool examination

Urine

Urinalysis, urine microscopy and culture are general tests that tend to be undertaken for patients who have pyrexia, general malaise and vague abdominal pain and in cases of amoebiasis in pregnancy, the results would tend to be normal unless there is an additional urinary tract infection.

Haematology Blood Tests

Routine haematology blood tests form part of the general laboratory tests that are undertaken in the assessment of patients that have amoebiasis and in some cases there would tend to be leucocytosis. But leucocytosis would not be diagnostic of amoebiasis and at times when there is leucocytosis clinicians would tend to wonder if there is a bacterial infection.

Biochemistry Blood Tests

Routine biochemistry blood tests including serum urea and electrolytes, Estimated glomerular filtration rate (EGFR), blood glucose, and liver function tests tend to be undertaken as part of the general assessment of patients who have amoebiasis and depending upon the stage of the infection the results could be normal and in cases of dehydration there could be evidence of impaired renal function and reduced EGFR. Elevated levels of liver enzymes may be seen in some cases of amoebic liver disease and amoebic liver abscess.

Polymerase Chain Reaction (PCR) Assays

PCR assays are routine reliable tests that tend to be undertaken to establish the diagnosis of amoebiasis in the developed world including United States of America, Canada and Western Europe, Australia, New Zealand, and Japan, as well as in well equipped and well resourced hospitals of the tertiary hospitals of the developing world.

Radiology Imaging

Ultrasound scan:

- Ultrasound scan of abdomen and pelvis does form part of the standard investigation / assessment of patients who have amoebiasis of the liver and this would illustrate whether there or there is no abscess within the liver. If there is abscess within the liver the ultrasound scan would indicate whether there is one abscess or more than one abscess within the liver. The ultrasound scan would also indicate the features of the abscess or abscesses, the location as well as the size or sizes of the abscess or abscesses.
- Ultrasound scan-guided aspiration of a hepatic amoebic abscess plus / minus insertion of a percutaneous drain into the abscess cavity can be undertaken and ultrasound scan biopsy specimens can be obtained from the liver lesion under ultrasound scan guidance.
- Contrast-enhanced ultrasound (CEUS) can be undertaken in radiology departments that are able to perform CEUS to assess in detail amoebic liver abscesses.
- Ultrasound scan of abdomen and pelvis has tended to be very useful in the monitoring of patients who are undergoing drainage of amoebic abscesses to ascertain if there is complete resolution of the abscess so that the drain can be removed.
- During the follow-up assessment of individuals who have completed treatment of their previous amoebic abscess or abscesses of the liver regular follow-up ultrasound scan of the abdomen and pelvis tends to be undertaken to ascertain if there is or there is no recurrence of the liver abscess.
- Ultrasound scan of abdomen and pelvis in cases of amoebiasis of the liver associated with pregnancy would ascertain if there is intra-uterine growth retardation or not of the foetus taking into consideration the gestational age of the patient.

Magnetic Resonance Imaging (MRI) scan

- MRI scan of abdomen and pelvis could be undertaken in the investigation / assessment of patients who have amoebiasis of the liver and this would illustrate whether there or there is no abscess within the liver. If there is abscess within the liver the ultrasound scan would indicate whether there is one abscess or more than one abscess within the liver. The MRI scan would also indicate the features of the abscess or abscesses, the location as well as the size or sizes of the abscess or abscesses.

- MRI scan-guided aspiration of a hepatic amoebic abscess plus / minus insertion of a percutaneous drain into the abscess cavity can be undertaken and MRI scan biopsy specimens can be obtained from the liver lesion under ultrasound scan guidance.
- Contrast-enhanced MRI (CEMRI) scan would reveal detailed features of the amoebic liver abscess or abscesses.
- MRI scan of abdomen and pelvis can be used in the monitoring of patients who are undergoing drainage of amoebic abscesses to ascertain if there is complete resolution of the abscess so that the drain can be removed. Nevertheless, MRI scan tends not to be readily available in many hospitals globally especially within district hospitals in developing countries.
- During the follow-up assessment of individuals who have completed treatment of their previous amoebic abscess or abscesses of the liver regular follow-up MRI scan of the abdomen and pelvis can be undertaken to ascertain if there is or there is no recurrence of the liver abscess.
- MRI scan of abdomen and pelvis in cases of amoebiasis of the liver associated with pregnancy would ascertain if there is intra-uterine growth retardation or not of the foetus taking into consideration the gestational age of the patient.

Computed Tomography (CT) Scan

- CT scan of abdomen and pelvis can be undertaken in the investigation of a suspected amoebic liver abscess only in a woman who is not pregnant because of the radiation effect of CT scan. Therefore in cases of pregnant ladies CT scan tends not to be undertaken.

Colonoscopy

In cases of bloody stools, apart from microscopy examination of stools, and stool culture, rectal examination and colonoscopy tends to be undertaken with biopsies of any unusual looking areas of the rectum and large bowel for histopathology examination to exclude malignancy and ulcerative colitis and in cases of amoebic dysentery this will be demonstrated upon pathology examination and malignancy as well as ulcerative colitis would be excluded based upon pathology examination features of the biopsy specimen.

Diagnosis [11]

- It has been iterated that usually entamoeba tends to be detected within the stool ova and parasite examination [11]
- It has been documented that many authorities have recommended the utilization of antigen detection or PCR based assays to differentiate *Entamoeba histolytica* from non-pathogenic amoeba [11] [32]
- It has been stated that amoeba could be seen within tissue biopsy material [11]
- It has been iterated that patients who have amoebic liver abscesses usually tend to have anti amoebic antibodies and amoebic antigen within their serum [11]
- It has been stated that aspiration of cyst sometimes tend to be undertaken and even though it is unusual to see parasites, the absence of other microorganisms is supporting evidence of amoebic liver abscess [11]

Radiology imaging guided aspiration / biopsy

Radiology image-guided aspiration of abscess within the does serve the dual purpose of obtaining samples of the abscess for pathology examination including microbiology microscopy and culture examination and pathology examination, as well as it does provide treatment to remove the abscess and in cases of residual abscess, radiology image-guided (ultrasound scan-guided or MRI scan-guided) insertion of a Percutaneous drain into the abscess cavity can be undertaken and any abnormal looking areas of the wall of the cyst or liver can be biopsied for pathology examination.

Laparoscopy / Laparotomy Aspiration / Biopsy

Laparoscopy can be done in some cases to establish diagnosis and during the procedure, laparoscopic-guided aspiration of a liver abscess/cyst can be undertaken as well as insertion of a per-cutaneous drain which would provide treatment. Globally there are are not very many laparoscopy surgeons, especially within the developing countries and therefore laparoscopy would tend to be undertaken only in centres that have the facilities and well-trained staff and within the less-resourced hospitals laparotomy would tend to be undertaken as may be required.

Treatment

A number of anti-amoebic medications exist but the most commonly utilized medication is metronidazole which summations as follows: [11]

- Metronidazole
 - *Entamoeba histolytica* is stated to lack mitochondria and is an obligate fermenter of glucose
 - Metronidazole is stated to target ferridoxin-dependent pyruvate oxidoreductase necessary for fermenting glucose

Gross description

The macroscopic examination features of specimens of bowels that have been infected by amoebiasis have been summarized as follows: [11]

- Gross examination of the specimen does show discrete ulcers with normal intervening mucosa
- Gross examination of the colonic specimens that contain amoebic colitis might reveal areas of colitis or inflammatory polyp

Microscopic (histologic) description

The microscopy histopathology examination of specimens of the colon in cases of amoebic colitis has been summarized as follows: [11]

- It has been stated that amoeba does burrow into the lamina propria and does cause tissue necrosis with relatively little inflammation
- It has also been stated that early amoebic lesions of the colon do show scattered neutrophils
- It has been iterated that more developed cases of amoebic colitis generally demonstrate broad based "flask" shaped ulcers 1 to 2 mm in diameter upon microscopy examination
- It has additionally been iterated that microscopy pathology examination of specimens of amoebic colitis does tend to show that the trophozoites of *Entamoeba histolytica* are 6 to 40 nm and they mimic macrophages:
 - They are seen to be round to oval in shape and they could be encompassed by a halo

- The cytoplasm tends to be abundant and vacuolated and it could contain ingested red blood cells which indicate tissue invasion
- The nuclei tend to be small and round with prominent nuclear membranes as well as a central karyosome (chromocenter)
- They tend often to be found clustered at the luminal surface or within debris

- Tuberculosis
- Ulcerative colitis.

Cases of basal right basal pneumonia could also simulate infection in the sub-costal region one of which is liver abscess of which amoebic liver abscess is one of them.

Outcome

Once the diagnosis is established and treatment of amoebiasis in pregnancy is provided by appropriate anti-amoebic medication and aspiration / drainage of abscess is undertaken whether by means of radiology image-guided aspiration / insertion of a drain or by means of laparotomy and drainage of the abscess or abscesses, the eventual outcome tends to be good but treatment of delayed cases could be associated with more morbidity.

(B) Miscellaneous narrations and discussions from some case reports, case series, and studies related to amoebiasis in pregnancy.

Kaiser et al. [15] reported a 30-year-old Austrian lady, who was admitted as an emergency who has presented with a history of worsening abdominal pain within the right upper quadrant of her abdomen which had commenced over a period of the preceding one week. She was stated to be pregnant (5 weeks +3) which was confirmed by serum beta-human chorionic gonadotrophin (Beta-HCG) testing. Additionally she had other symptoms which included nausea, headache as well as progressive malaise. She did not have any significant past medical history and she had not been taking any medications. She had travelled frequently abroad over the preceding decade which did include travelling to prolonged journeys to South East Asia, Northern Africa and South America (Figure 1). It was noted that during a period of her five month stay within Indonesia seven years earlier preceding the onset of her symptoms, she was reported to have had an eight week-long episode of intermittent bloody diarrhoea.

Positive stains

Immunohistology staining studies of biopsy specimens from lesions of amoebiasis tends to show positive staining for: [11]

- PAS, and trichrome [11]

Negative stains

Immunohistology staining studies of biopsy specimens from lesions of amoebiasis tends to show negative staining for: [11]

- CD68. [11]

Differential diagnosis

Some of the differential diagnose of amoebiasis include: [11]

- Appendicitis
- Balantidium coli infection.
- Crohn’s disease.
- Histiocytosis (Histiocytes)
- Non-pathogenic amoeba
- Pseudomembranous colitis
- Pyogenic abscess within the liver

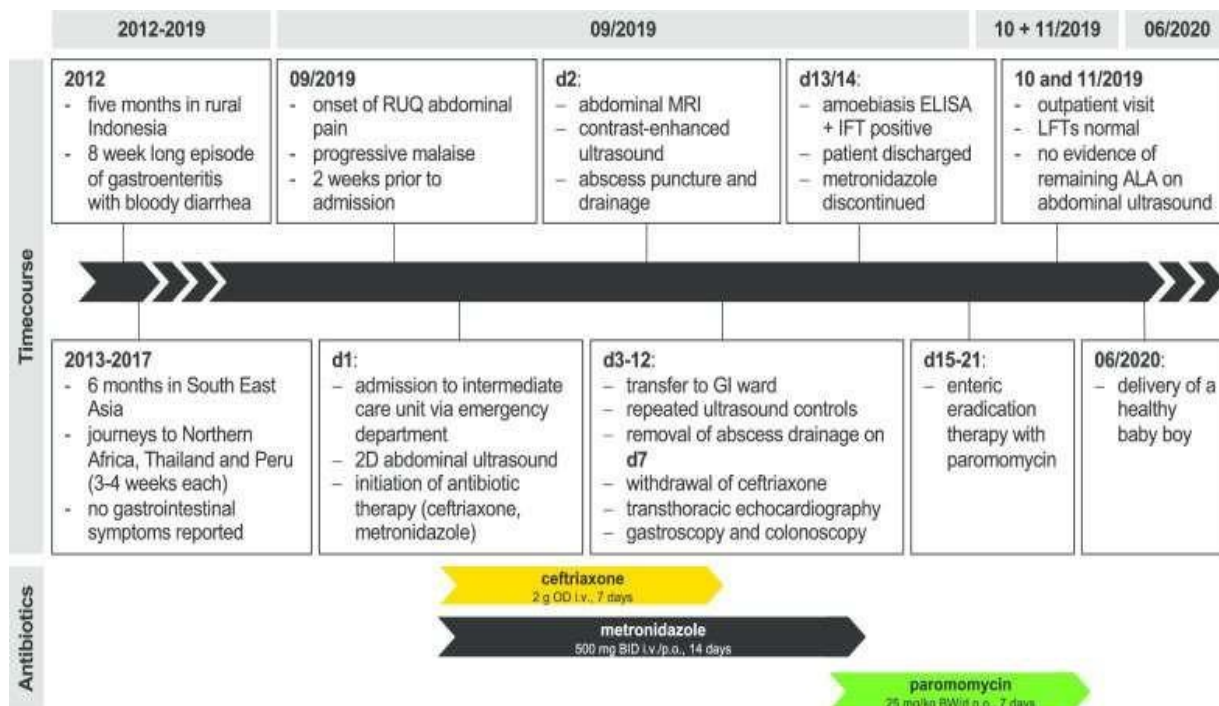


Figure 1: Time-course of the patient’s travel history as well as the pre-, intra-, post-hospital course of treatment.

Reproduced from: [15] Kaiser RWJ, Allgeier J, Philipp AB, Mayerle J, Rothe C, Wallrauch C, Op den Winkel M. Development of amoebic liver abscess in early pregnancy years after initial amoebic exposure: a case report. *BMC Gastroenterol.* 2020 Dec 14;20(1):424. doi: 10.1186/s12876-020-01567-7. PMID: 33317457; PMCID: PMC7734812. <https://pubmed.ncbi.nlm.nih.gov/33317457/> under copyright: © The Author(s) 2020. Open Access: This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Her general and systematic examinations were within normal range. She was found to be tender within the right upper quadrant of her abdomen. The results of her routine haematology and biochemistry blood tests were reported as follows: leucocyte counts 12 G/l which was raised (normal range [NR] 3.90 to 9.8 G/l); C-reactive protein (CRP,) 25.3 mg/dL, NR 0.5 mg/dL); as well as alkaline phosphatase (AP) 305 U/l, NR (40 – 130 U/l); as well as gamma glutamyl transferase (GGT), 142 U/l, NR (59 U/l); bilirubin levels were within normal range. She had ultrasound scan of her abdomen and pelvis which did not show any evidence of cholestasis but which demonstrated a 5 cm x 4 cm hypoechoic mass within segment V of the right lobe of her liver (see figure 2a). Her contrast-enhanced ultrasound scan (CEUS) demonstrated no evidence of central vascularization of the hepatic lesion, but it demonstrated a ring-like hypervascularization encompassing the mass, which was adjudged to be consistent with liver abscess (see figure 2b). She did not undergo CT scan in view of her young age as well as because of the fact that she was pregnant. She had non-contrast magnetic resonance imaging (MRI) scan of her abdomen and pelvis which revealed a T1 hypo—(see figure 3a) and T2-hyper-intense liver lesion that measured 4.6 cm with regard to its diameter which contained both solid as well as cystic components that contained suspected septa within the lesion and also restricted diffusion (see figure 3b). The radiology imaging features of the hepatic lesion were considered to suggestive of differential diagnoses that included: liver abscess, ruptured hydatid cyst, and an unlikely necrotizing malignant tumour of the liver.

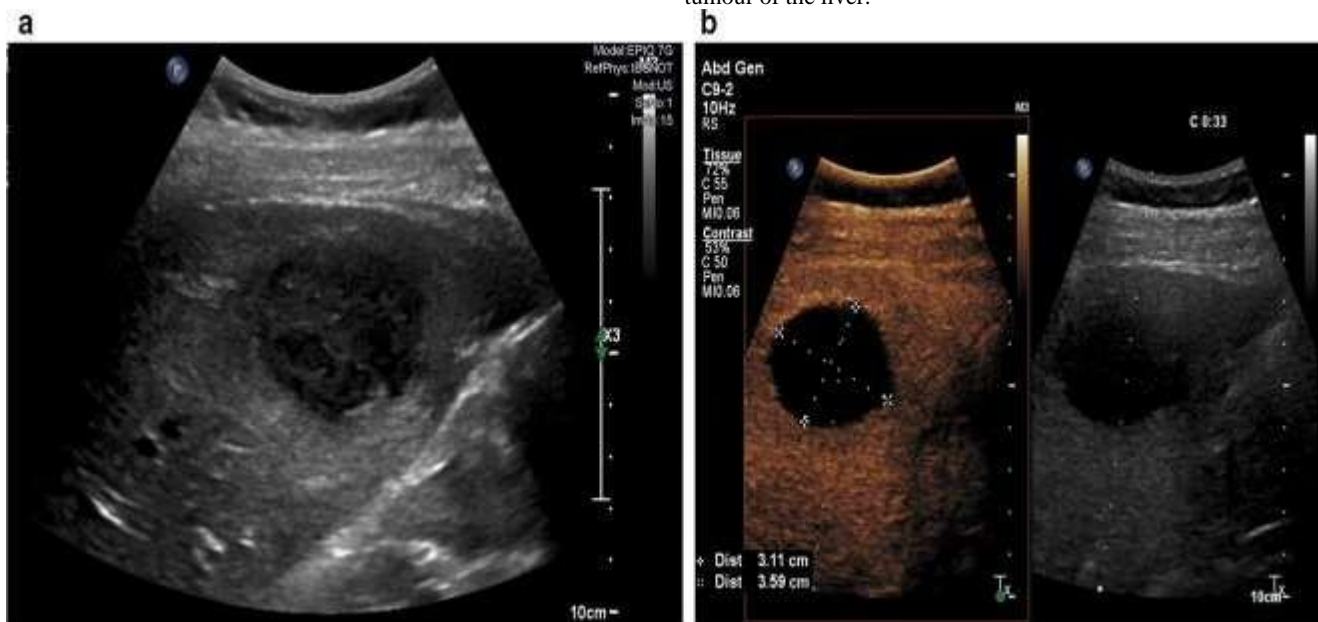


Figure 2: a 2D abdominal ultrasound performed on the day of presentation shows a hypoechoic, in-homogeneous, and approximately 4 x 5 cm large lesion in hepatic segment V. b Contrast-enhanced ultrasound of the liver reveals peripheral hypervascularization of the lesion in segment V without central uptake of contrast, a finding consistent with liver abscess.

Reproduced from: [15] Kaiser RWJ, Allgeier J, Philipp AB, Mayerle J, Rothe C, Wallrauch C, Op den Winkel M. Development of amoebic liver abscess in early pregnancy years after initial amoebic exposure: a case report. *BMC Gastroenterol.* 2020 Dec 14;20(1):424. doi: 10.1186/s12876-020-01567-7. PMID: 33317457; PMCID: PMC7734812. <https://pubmed.ncbi.nlm.nih.gov/33317457/> under copyright: © The Author(s) 2020. Open Access: This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party

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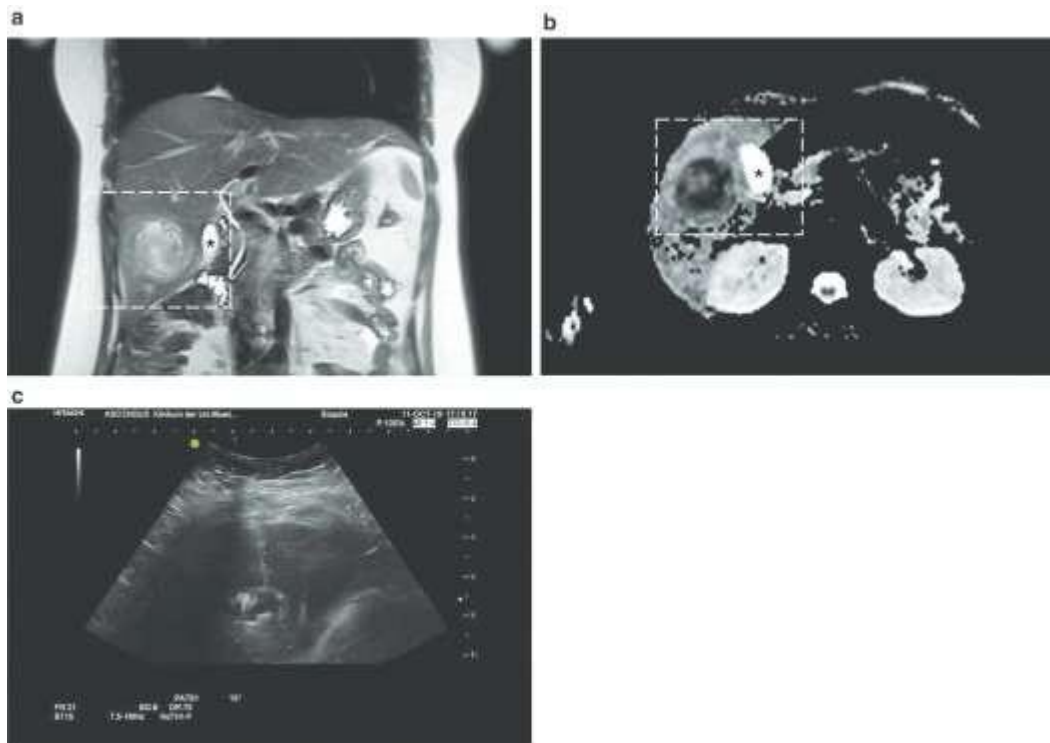


Figure 3: a: Coronal MRI image of the liver without contrast reveals a T1-Hyintense hepatic lesion, adjacent to the gall bladder (indicated with *). b: Axial MRI sequences showing diffusion restriction to the centre of the lesion (* = gall bladder). c: 2D sonography after successful transhepatic puncture drainage.

The green dots depict the direction of puncture, the hyperechogenic reflexes within the lesion are caused by the drainage. Reproduced from: [15] Kaiser RWJ, Allgeier J, Philipp AB, Mayerle J, Rothe C, Wallrauch C, Op den Winkel M. Development of amoebic liver abscess in early pregnancy years after initial amoebic exposure: a case report. *BMC Gastroenterol.* 2020 Dec 14;20(1):424. doi: 10.1186/s12876-020-01567-7. PMID: 33317457; PMCID: PMC7734812.

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After taking into consideration, the patient's history of travelling, extended serology testing for infectious disease was undertaken. The results of the serology tests did rule out *Echinococcus* spp as well as other parasites and tuberculosis as well as HIV infection. It did appear that the lesion was unlikely and hence an abscess of the liver was considered to be the most likely differential diagnosis.. An empirical treatment of metronidazole 500 mg intravenously twice per day and ceftriaxone 2

grams intravenously one per day was commenced. Ultrasound scan-guided puncture of the abscess with insertion of a 10 French (FR) drainage was undertaken (see figure 3C). The aspirate from the drainage fluid did appear to be brownish in colour and it did contain streaks of blood. Analysis of the fluid did show a high amount of both neutrophil as well as eosinophil granulocytes, as well as cultures from both the abscess fluid and the peripheral blood did not demonstrate any bacterial growth, fungi, or parasites. Furthermore, a PCR targeting prokaryotic 16S and fungal 18S/28S ribosomal RNA did not demonstrate any evidence of bacterial or fungal infection. Ensuuing her antibiotic treatment and algesia treatment, her general condition did improve. The results of her laboratory tests did demonstrate reduction of inflammatory markers and liver function tests (LFTs), and she had follow-up ultrasound scan of her abdomen which demonstrated shrinkage of the abscess. Six days following insertion of her drain, the per-cutaneous drain was removed. She additionally had trans-thoracic echocardiography, gastroscopy and colonoscopy which were all normal and which did exclude extra-hepatic manifestations of infection as well as underlying malignancy. Positive amoebic serology was shortly after was obtained based upon both amoebiasis -EIA (enzyme immunoassay; 100 U, NR < 10 U); as well as amoebiasis immunofluorescence (IFT) testing, 1:128, NR < 1.64). Ceftriaxone treatment was stopped and she was continued on metronidazole treatment for a total duration of 14 days (see figure 1). In order to reduce recurrence of the abscess, based upon a multi-disciplinary team meeting discussion of clinicians including clinical pharmacology clinicians, infectious diseases team, and the gynaecology team, she was commenced on a one week treatment of intraluminal acting aminoglycoside paromomycin 25 mg /kg body weight per day. She was subsequently discharged pursuant to her continued clinical improvement. During two week- and four-week – follow-up assessments she was found to be in excellent condition. The results of her routine haematology and biochemistry blood tests during the follow-up assessments demonstrated almost complete normalization of her LFTs, normal white blood cell count and CRP levels, as well as

concomitant increase in the level of her Beta-HCG. She had ultrasound scan of her abdomen which demonstrated complete regression of her abscess and she also had trans-vaginal ultrasound scan which showed normal embryonic development. She did not experience any adverse reactions to her antibiotic therapy throughout her pregnancy as well as no clinical signs of relapse of amoebiasis developed. She delivered a healthy normal child seven months pursuant to her discharge.

Cowan [33] stated that the association between amoebiasis of the liver and pregnancy is uncommon and that between 1966 and 1976, only 5 cases amoebiasis of the liver and pregnancy had been reported in the world literature. Cowan [33] reported the 6th case of amoebiasis of the liver associated with pregnancy in 1978 Cowan et al. [33] reported a 30-year-old black woman who was admitted to the Department of Obstetrics and gynaecology of King Edward VIII Hospital in Durban South Africa on the 21st of November 1976. She was stated to have apparently given birth on the 18th of November 1976 at home. She was found upon admission to be semi-conscious confused as well as not able to communicate coherently. She was also noted to be grimacing spasmodically as well as groaning. Her temperature on admission measured 39 degrees centigrade and her heart rate was 150 beats per minute. Her blood pressure measured 120/80 mm Hg. Her neck was supple and not stiff. During her abdominal examination, it was noted that she had generalized abdominal tenderness as well as guarding and rebound tenderness.. Her uterus was not palpable during her abdominal examination. Upon auscultation of her abdomen it was noted that there was absence of bowel sounds. Upon her vaginal examination, it was noted that her cervix was widely dilated and healthy. Products of conception was not felt during her examination. Products of conception could not be felt. Digital rectal examination showed a brown liquid stool with no evidence of blood or mucus. Ascaris infestation and segments of Taenia coli were observed. The results of her routine haematology and blood tests revealed haemoglobin level of 14,1 g/dl, and white cell count of 17000/I.t.l, as well as serum urea and electrolyte values were within normal range. She was resuscitated with intravenous fluids, as well as she was treated with antibiotics and she underwent laparotomy. She underwent a sub-umbilical midline incision which was extended up into her epigastrium. A thin yellowish intraperitoneal pus was found within her lower abdomen. Her uterus, fallopian tubes as well as her ovaries were found to be normal. Her small bowel as well as her large bowel were also normal. A ruptured abscess was found within the left lobe of her liver, with widespread intraperitoneal soiling. The liver abscess cavity was 14 cm in diameter. The rest of the liver was normal and no further abscesses were found. Filmy adhesions were observed between the upper surface of her liver and the lower surface of her diaphragm. A biopsy specimen was obtained from the cavity of the abscess, one to the right sub-phrenic space, and peritoneal lavage was undertaken with saline and kanamycin. At the end of the operation, tube drains were inserted as follows: one drain was inserted into the abscess cavity, one drain was inserted into her right sub-phrenic space, one drain was inserted into her left para-colic gutter, and one drain was inserted into her pouch of Douglas. Her laparotomy wound was closed in layers, with tension sutures. Post-operatively, the patient received intravenous fluids and nasogastric drainage. She also received treatment with ampicillin 500 mg every 6 hours, kanamycin 500 mg every 12 hours, as well as dihydro-emetine 90 mg daily intramuscularly. She was digitalized and had regular monitoring of her oral fluid intake and central venous pressures. When she started having good oral intake her hydro-emetine medication was changed to oral metronidazole 800 mg every 8 hour. Her lower abdominal drains were removed on the 7th post-operative day. The abscess cavity drain as well as her subphrenic drain were removed on the 14th post-operative day. She was discharged home after her temperature had remained normal for one week and there was no evidence of discharge from her drain sites. At her 3 months follow-up, she had remained asymptomatic with no evidence of residual disease.

Histopathology examination of the wall of the abscess cavity showed presence of Entamoeba Histolytica and a probable secondary infection. Her gel diffusion test result was strongly positive.

Cowan et al. [33] summated some of the salient points related to amoebiasis as follows

- Homer and McNal [34] reported a greatly increased mortality from amoebiasis in pregnancy.
- It has been postulated that the increased susceptibility of pregnant women to the development of Entamoeba. histolytica is related to a defective immune response or to altered hormonal status of the pregnant lady. Nevertheless, Entamoeba. histolytica is commonest pathogenic parasite that is encountered within temperate climates, and the parasitic role of Entamoeba histolytica in man is increasing. In view of this it is a surprise that pregnancy that is complicated by amoebiasis is not encountered frequently within their hospital, where about 20000 deliveries tend to be undertaken each year, and that amoebiasis of the liver during pregnancy had only been reported five times globally within the preceding 10 years. Additionally, maternal death due to amoebiasis within their hospital was rare.
- It could be that the greatly increased mortality which was reported Abioye and Edington6 [35] was attributable to the socio-economic conditions that were prevailing within West Africa at the time of their study.
- Out of 5 cases of amoebiasis that had been reported within the English literature with the inclusion of their reported case, the right lobe of the liver had been involved thrice (3 times) by single abscesses, and once by multiple abscesses. With regard to their reported case, only the left lobe of the liver was involved with a single abscess. This does follow the distribution of amoebic liver abscesses that were seen in the post-mortem examination series of Abioye and Edington: [35].
- Intra-peritoneal rupture of the amoebic hepatic abscess had occurred in 3 of the previously reported cases. Rupture after birth was found in their reported case as well as by Navaratne [36]. Rupture during birth of a baby did occur in the patient who was reported by De Silva [37]. No rupture of amoebic abscess was seen by Wagner et al [38] regarding the 2 cases they had reported.
- In the scenario of suspicion of an unruptured amoebic hepatic abscess, they would recommend that clinical examination as well as a gel diffusion test be undertaken and this should be followed by ultrasound scan localization of the abscess and this should be ensued by trans-abdominal aspiration of the abscess, as was undertaken by Adams and MacLeod [39]. Amoebicidal treatment with utilization of metronidazole should be commenced contemporaneously.
- Ultrasound scan of the liver does tend to be particularly advantageous during pregnancy because ultrasound scan does obviate utilization of radioactive isotopes.
- It is important to identify the syndrome of 'pre-rupture' of an amoebic hepatic abscess. It has been stated that pre-rupture of amoebic liver abscess in does exist when the patient manifests with abdominal signs of localized peritonitis, but during laparotomy in such cases. no peritoneal contamination tends to be seen. Invariably this type of case has tended to be because of a superficial abscess within the right lobe of the liver with

fibrinous adhesions between the visceral and parietal peritoneum over the site of the abscess. If the syndrome is recognized and appropriate drug treatment is provided, a laparotomy could be avoided.

- They would recommend that, when a ruptured amoebic hepatic abscess has been diagnosed, then surgery should be undertaken. Laparotomy and drainage of the hepatic abscess with tube drains should be undertaken pursuant to vigorous resuscitation. When the patient is not able to take oral preparations, dihydroemetine or intramuscular metronidazole should be utilized. When the patient is able to take medications orally, metronidazole 800 mg, 8 hourly should be given and broad-spectrum antibiotics should also be given in order to prevent secondary infection.

Constantine et al. [40] reported a lady who had developed amoebic liver abscesses during her pregnancy and who subsequently developed amoebic peritonitis. Constantine et al. [40] iterated that it was their belief that their reported case of the development of amoebic infections of the liver during pregnancy that was ensued by the development of peritonitis was the first case to be reported within the United Kingdom as well as it was unusual that the lady had never travelled abroad. They additionally iterated that even though amoebiasis often tends to be considered a disease of the tropical countries and sub-tropical countries, amoebiasis also does occur elsewhere outside the tropical and sub-tropical countries. Constantine et al. [40] also stated the following:

- Whilst the patient who develops amoebiasis has usually travelled abroad in the past, travelling does not need to have taken place before an individual develops amoebiasis.
- Pregnancy does lower the immunity to the development of many parasitic infections that include amoebiasis and in view of this patients who have subclinical infestations could develop clinical symptoms during their pregnancy as they had described in their reported case.

Constantine et al. [40] reported a 22-year-old white lady who was 13 weeks pregnant in her second pregnancy attended for assessment. Her general examination and her routine investigations were all normal. She was noted during the 28 weeks assessment to have a static weight; nevertheless, she was otherwise well and asymptomatic. By the time of her 32 weeks pregnancy, she had not gained any maternal weight and she had clinical intra-uterine growth retardation which was confirmed based upon ultrasound scanning. She was admitted one week later, as an emergency when she presented with right sided pleuritic chest pain that was associated with dyspnoea and tachypnoea. She was found to be apyrexial and she had tachycardia. The result of her white blood cell count was $10.3 \times 10^9/l$. She had a chest radiograph which demonstrated a slight elevation of her right hemi-diaphragm. A definitive diagnosis could not be made but her symptoms did resolve over the ensuing 24 hours. On the 4th day pursuant to her admission, she started to vomit as well as to pass blood-stained diarrhoea stools. Based upon a second opinion that was provided by a gastroenterologist, a tentative diagnosis of Crohn's disease was made and she was started on steroid enemas. Her general condition did stabilise; nevertheless, she had continued to pass blood via her rectum and therefore she was commenced on ACTH injections. She did not have any evidence of pyrexia or septicaemia. On the 5th day pursuant to her admission she did develop generalized tenderness within her abdomen and went into spontaneous labour. In view of the transverse lie of the baby, an emergency caesarean section was undertaken. A live infant was delivered and the baby weighed 1.92 kilograms. During the operation, pus was found within her right --+para-colic gutter which was related to two liver abscesses within the right lobe of her liver, as well as her colon was found to be dilated as well as inflamed. A defunctioning caecostomy was

undertaken and her hepatic abscesses were drained. She underwent sigmoidoscopy which demonstrated a normal rectum macroscopically and a biopsy was taken for pathology examination. He was started on Gentamicin and metronidazole. The preliminary diagnosis was that of inflammatory bowel disease with secondary liver abscesses. She did remain stable over the ensuing 24 hours; however, she developed pulmonary oedema, cyanosis, oliguria, as well as shock.

She required intensive care supportive treatment that required her to be ventilated as well as given inotropes from which she was weaned off 10 days after her delivery. Microscopy examination of the pus and of her rectal biopsies demonstrated presence of *Entamoeba Histolytica*; even though her cultures did not grow any organism. She was discharged home on the 47th day pursuant to her admission and 42 days pursuant to her delivery of her baby. Constantino et al. [39] made the ensuing iterations about amoebiasis within the United Kingdom:

- It has been estimated that within the United Kingdom, there are approximately 3 deaths and 200 new cases of amoebiasis per year.
- Cases of amoebiasis of the liver which had been reported within the United Kingdom had been virtually reported in men only and not in women and many of these men, although not all of them had travelled abroad at some stage of their life. [41]. [42.]
- Some patients who had amoebiasis had never travelled abroad and other patients who had amoebiasis considered to have contracted amoebiasis from relatives who may have travelled abroad. [43].
- The case of amoebiasis they had reported was unusual in that she had never travelled abroad and none of her relatives had travelled abroad. The time during which she did acquire the amoebiasis was not known in view of the fact that amoebiasis can remain quiescent for several years and based upon her background history she must have acquired the amoebiasis within the United Kingdom.
- It has been documented that amoebiasis has tended to be more severe in pregnant women.[35, 44, 45]
- The fact that amoebiasis is considered to be more severe in pregnant women has been conjectured to be related to the raised levels of progesterone in pregnant women [8] [46], as well as due to the failure of immunoglobulin levels to be elevated during infection. [35].
- With regard to their reported case, immunoglobulin levels of the patient were within the normal range.
- The occurrence of amoebic dysentery during pregnancy had been extensively reported within the literature and amoebic liver abscess in pregnancy had been reported less often. Cases of amoebiasis associated with pregnancy had all been reported from areas of the world where amoebiasis might be expected to be relatively commonly encountered. [45, 47].
- It was their opinion that their patient was the first case of amoebiasis in pregnancy to be reported in the United Kingdom.
- In virtually all of the aforementioned previously reported case of amoebiasis in pregnancy, mis-diagnosis had occurred, and with regard to many of the cases the diagnosis was established during laparotomy.
- It has been iterated that involvement of the intestine has tended not to be universal in amoebiasis of the liver in view of the fact

that 30% to 50% of patients who have hepatic amoebic abscesses have been documented not to have any bowel related history [35].

- With regard to their reported case, some, but not all, of the typifying features of amoebiasis of the liver were present and this would be indicative of the fact that clinicians need to have a high index of suspicion for amoebiasis when patients do manifest with right sided chest pains and tenderness, or weight loss, even if they are afebrile and they do not have any bowel related symptoms.
- Their reported case had illustrated the need to exclude positively an infestation/infection before making a diagnosis of Crohn's disease or ulcerative colitis and providing treatment for these.
- The combination of severe amoebic colitis, contemporaneously with a ruptured liver abscess does appear to be uncommon in the cases of amoebiasis in pregnancy that previously been reported. This could have contributed to the patient's stormy postoperative recovery in comparison previous cases of amoebiasis in pregnancy that had previously been reported.
- With regard to non-pregnant patients who had ruptured liver abscesses, an overall mortality of 42%, which had increased with age as well as delay in diagnosis had been reported [48].
- Considering that partially individuals who had developed amoebiasis in pregnancy had been debilitated, their post-operative morbidity had tended to be high and for this reason clinicians who encounter patients who develop amoebiasis in pregnancy should anticipate high post-operative morbidity
- Cardiovascular as well as respiratory tract problems, metabolic disorders, renal failure, as well as shock had all been described related to amoebiasis in pregnancy which could require the support and treatment by specialists.
- With regard to uncomplicated cases of amoebic dysentery as well as small hepatic amoebic abscesses utilization of metronidazole alone could provide effective treatment.
- With regard to larger unruptured amoebic abscesses, trans-abdominal aspiration of the abscess, could be attempted but in cases of suspicion of a ruptured amoebic abscess, it has been

stated that laparotomy would be necessary and would provide lifesaving treatment. [35] [41].

- They had highlighted the possibility of patients within the United Kingdom acquiring and developing amoebiasis of the liver, as well as they had highlighted the particular dangers of pregnancy, and the potential life-threatening complications that could occur if appropriate treatment of the disease is delayed.

Abioye and Edington [35] reported their study of the pathology of amoebiasis which had involved 7,922 necropsies undertaken within the University College Hospital, Ibadan in Nigeria. They reported that Amoebiasis did account for death in 135 subjects that amounted to 1.9%. They furthermore reported the following:

- The most common complications amoebiasis in their study were liver abscess and peritonitis.
- There was a significant increased frequency of amoebiasis in pregnancy in comparison with non-pregnant females.

Abioye and Edington [35] additionally, iterated that ulcerative post-dysenteric colitis could be more frequent than their study had suggested.

Karadbhajnne et al. [49] reported a 28-year-old woman who was 30 weeks pregnant who had manifested with abdominal pain and bloody diarrhoea. After her examination up to 27 weeks of her gestation, she was noted to have had a steady weight and all her pulse, and heart rate were normal. She has had her symptoms over the preceding 10 days. She was asymptomatic otherwise in that she did not have any fever, white discharge or any other complaints. She did not have any significant past surgical history. A stool sample was obtained from her which was examined under microscope that showed eggs.

From her stool sample extraction of DNA was undertaken by utilization of Hi-media kit and RT-PCR was undertaken. The sample was positive for Entamoeba Histolytica infection. The 20µl reaction mixture for RT-PCR was utilized as follows: 1x Tag man mixture, forward primer, reverse primer, probe, nuclease-free water, DNA. RT-PCR is a molecular technique that is a more reliable and accurate technique to diagnose the disease. RT-PCR reaction curve graph is given in figure-5. Several visits were made to her household pursuant to her observation for 7 days during which period she did not have any abdominal pain or bloody diarrhoea. She also did not develop any new symptoms.

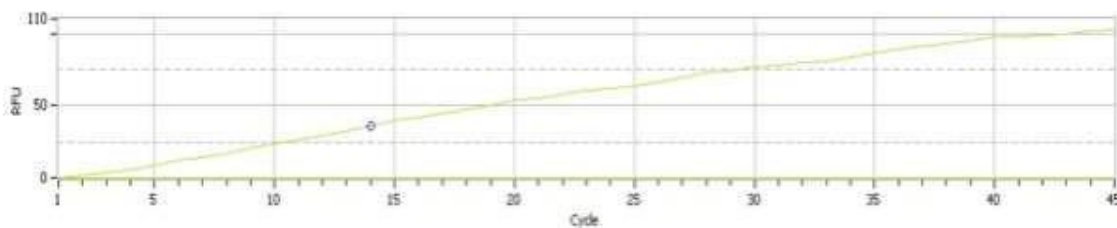


Figure 5: Reaction curve graph of RT-PCR assay.

Time line

The regular visit to their household was done, after 7 days of observation; there was no abdominal pain and bloody diarrhoea. No new symptoms were seen in woman.

Reproduced from: [49] Karadbhajnne P, Tambekar A, Gaidhane A, Quazi Syed Z, Gaidhane S, Patil M. Amoebiasis in pregnant woman: A case report. Medical Science, 2020, 24(104), 1814-1817]

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Karadbhajnne et al. [49] made the ensuing summing discussions:

- Intestinal Protozoan infections tend to be closely related to a lack of proper sanitation as well as environmental contamination with faecal material.
- Amoebiasis is a potentially severe as well as a life-threatening infection which is caused by an enteric protozoa.
- During pregnancy, the amoebic disease does appear to be very frequently associated with low immunity.
- An amoebiasis infected pregnant lady does tend to develop bloody dysenteric stools with moderate abdominal pain and abdominal tenderness.
- Early precise diagnosis of amoebiasis in pregnancy of the patient would be life-saving in the case of *Entamoeba histolytica*.
- Amoebiasis could remain dormant or it could increase from days to years pursuant to the initial infection and it does tend to be characterized by abdominal pain and bloody diarrhoea.
- It has been iterated that meals together on a dining plate by family members, had tended to help or to be responsible for the transmission of *Entamoeba histolytica* infection (Khanam et al., 2019). [50]
- It has also been iterated that with regard to the case of Amoebiasis, the sexual partner does need to be identified and treated in order to avoid recontamination (Zodpey et al., 2018). [51]
- If the individual who has amoebiasis had not travelled to an amoebiasis endemic area, then the person could have developed amoebiasis because of contamination with eggs of *Entamoeba histolytica*.
- It had been stated for the early detection of *Entamoeba histolytica* infection, a high sensitive molecular diagnostic method should be utilized in order to avoid unnecessary surgery and complication in the future delivery. [10]
- In a previous study some oral anal sexual transmission of *Entamoeba histolytica* infection had been reported. [52]
- It has been stated that for the control of transmission and prevention of amoebiasis the treatment of the patient is important whether symptoms are indicative or not of the disease [53].
- It had also been stated that the number of false positive amoebiasis result could be lower by utilization of improved molecular techniques such as RT-PCR and that this is better in comparison with the result of earlier disease identification theory. [40]

Karadbhajne et al. [49] made the following conclusions:

- *Entamoeba histolytica* does produce amoebiasis like disease in pregnant women who live within rural and urban area where sanitation problems do exist.
- *Entamoeba histolytica* is caused by the drinking of un-boiled water and food.
- Pregnant ladies need to take precaution at the time of drinking of water, it will be helpful for the avoidance of preterm delivery.
- RT-PCR was found to be more sensitive than microscopic examinations in their reported case.

Conclusion

- Amoebiasis is a common global diseases which is more common in amoebiasis endemic developing countries and which sporadically is reported in developed countries related to foreign travel to developing countries and contact with an amoebiasis infected individual who has travelled from a developed country to a developing country.
- Because generally amoebiasis in pregnancy is not well known and because amoebiasis whether it associated with pregnancy or not does present with non-specific symptoms, without a high index of suspicion for a possible amoebiasis, the diagnosis of amoebiasis has tended to be delayed or there has been misdiagnosis of amoebiasis on some occasions which has led to complications of amoebiasis including amoebic liver abscess, perforation of colon, perforation of the liver abscess and peritonitis which has led to increased morbidity and growth retardation / small for dates baby/foetus.
- If clinicians have a high incidence of suspicion for amoebiasis in pregnancy because they know that the condition exists this would enable them to undertake appropriate tests that would enable them quickly confirm the diagnosis as well as to commence correct appropriate treatment of the disease that would lead to a quick recovery of patients.

Conflict of Interest - None

Acknowledgement

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