

The Outcomes of Pregnancy in Patients with Cirrhosis in a Low-Income Country

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Abstract

Pregnancy in cirrhotic-woman is a rare event [1] [2]. It causes particular risks related to liver disease and its treatments, with maternal and fetal consequences. The largest reported series to date is by Welton's with 13 cases [3]. In Africa, few cases were reported. The purpose of this work was to report the hepatic and obstetric complications in pregnant women in Burkina Faso, a low-income country. It was a descriptive cross-sectional study with retrospective data collection covering the period from January 1, 2013 to December 31, 2023. All the women diagnosed with cirrhosis through clinical basis, biological and imaging arguments associated with a pregnancy confirmed by ultrasound were included. A total of ten women were included in the study. Among them, two were known cirrhotics and were being followed. In the other eight cases, cirrhosis was discovered during pregnancy. Eight women were HBsAg positive and two of them had only the contact marker of hepatitis B virus (anti-HBc antibody). The evolution was, ascitic decompensation in nine cases, digestive hemorrhage due to rupture of esophageal varices in two cases, nine cases of anemia, two cases of ascitic fluid infection and one case of conjunctival jaundice. Two cases of probable hepatocellular carcinoma were noted with one case of extensive portal thrombosis. The evolution was without maternal complications in one case. Regarding fetal and neonatal complications, there were three cases of hypotrophy, one case of prematurity, one case of acute neonatal distress, two cases of fetal death in utero and one case of fetal tachycardia. Four pregnancies had a favorable evolution without any complications. The association of cirrhosis and pregnancy is an uncommon event, and maternal and fetal complications can occur, making this pregnancy a high-risk pregnancy.

Keywords

Cirrhosis, Pregnancy, Complications, Burkina Faso

1. Introduction

The association of cirrhosis and pregnancy is an uncommon event. It causes particular risks related to liver disease and its treatments, with maternal and fetal consequences. The largest reported series to date is by Welton's with 13 cases [3]. In Africa few cases were reported, Sermé in Burkina Faso reported five cases [4]; Diarra in Mali reported one case [5]; N'Guessan in Ivory Coast, one case [6]; Dridi in Morocco one case [7]; and Ndubuda in Nigeria three cases [8]. The purpose of this work was to report the hepatic and obstetric complications in pregnant women in Burkina Faso, a low-income country.

Cirrhosis, an advanced stage of hepatic fibrosis, is the consequence of any chronic liver disease. It is a mutilating fibrosis of the liver, leading to the destruction of the hepatic parenchyma and the formation of regeneration nodules [9]. It is a serious, progressive disease and poses, due to its frequency, a real public health problem in the world, particularly in Africa. To date, the mortality and morbidity of this condition remain high. The prevalence and incidence of cirrhosis in the world are not precisely known. The main causes in France are distributed as follows: Alcohol 50% to 75%; Hepatitis C Virus (HCV) 15% to 25% and Hepatitis B Virus (HBV) around 5%. In developing countries, particularly in Africa, this condition seems to be linked to viral hepatitis, chronic alcoholism and malnutrition [10]. Indeed, Africa is considered, along with Southeast Asia, to be a highly endemic area where the prevalence of chronic hepatitis B virus infection is at least 8% [11].

In Burkina Faso, carriage of hepatitis B surface antigen (HBsAg) is high with a prevalence of 9.1%, despite the existence of effective vaccines that should help reduce the incidence of chronic liver disease due to the hepatitis B virus [12]. As a chronic disease, cirrhosis can be associated with the occurrence of pregnancy in women. Pregnancy is a physiological state characterized by the presence and then development of the product of conception, it continues until its expulsion. Liver diseases observed during pregnancy can be classified into three groups, namely [13]:

- gravidic liver disease which are linked to pregnancy in a specific way;
- episodic liver diseases that occur incidentally during pregnancy;
- and chronic liver diseases pre-existing to pregnancy which may be revealed by pregnancy or diagnosed incidentally during pregnancy. This is the case of cirrhosis.

Most women with mild chronic liver disease, especially viral, can carry a pregnancy to term. However, pregnancy in women with cirrhosis is a rare event. This

is due to the often-advanced age at the time of the development of cirrhosis and hormonal disorders with resulting subfertility [13]. Indeed, cirrhosis causes endocrine disorders that slow down ovulation, leading to disorders ranging from menstrual irregularity to persistent amenorrhea, responsible for subfertility. The frequency of metrorrhagia, changes in the hormonal cycle, and menstrual disorders explain the subfertility of women with cirrhosis [14]. The association of cirrhosis and pregnancy generates specific risks related to liver disease and its treatments with maternal and fetal consequences. According to literature data, the fetal risk is greater with a higher incidence of spontaneous abortions, premature deliveries, intrauterine growth retardation and fetal deaths. The main maternal complications are related to portal hypertension and the risk of hemorrhage. Although the increase in portal hypertension during pregnancy is not perfectly demonstrated, there is an undeniable excess morbidity, mainly in cases of advanced cirrhosis which justifies the notion of a high-risk pregnancy and requires multidisciplinary management [14] [15]. Only a few cases or case series exist in the literature [4]-[8] [16]. To date, only one study has been conducted on the association of cirrhosis and pregnancy in Burkina Faso and reported five cases over a three-year period from 2014 to 2016 [4]. The objective of our study was to study cirrhosis and pregnancy at the Yalgado OUEDRAOGO University Hospital Center (CHU-YO).

2. Patients and Methodology

The study was carried out in the Hepato-gastroenterology, Gynecology-Obstetrics and Neonatology departments of the Yalgado Ouédraogo University Hospital (CHU-YO) in Ouagadougou, Burkina Faso.

This was a descriptive cross-sectional study with retrospective data collection covering the period from January 1, 2013 to December 31, 2023. The study included all cirrhotic patients who were pregnant during the study period. This was a comprehensive sample of all cases of associated cirrhosis and pregnancy during the study period. The study included all patients diagnosed with cirrhosis. Cirrhosis was established on the basis of the following arguments:

- Clinical: edema-ascitic syndrome, heterogeneous hepatomegaly with sharp lower edge or atrophic liver.
- Biological: hepatocellular insufficiency syndrom.
- Imaging (ultrasonography, tomography or MRI) suggestive of cirrhosis.

The pregnancy was clinically suspected and confirmed by ultrasound.

Patients with incomplete clinical records were not included. Data were collected using a semi-structured questionnaire that served as a guide. In an attempt to address the issue of our study, we chose to conduct a retrospective study based on a documentary review of clinical records and then conducted a telephone interview to obtain information on missing data. The study was carried out with the approval of the Headmaster of the hospital. Our data were collected while respecting the anonymity and confidentiality of the patients.

3. Results

In total, ten pregnancies occurred in ten patients with cirrhosis. Over the same study period, there were a total of 76,862 pregnancies, or 10 pregnant cirrhotic women out of 76,862 pregnancies. The mean age of the patients was 32.5 years with extremes of 26 to 38 years. All were married and housewives. Eight resided in rural areas and two patients in urban areas.

- No patient was vaccinated against hepatitis B.
- One patient had a history of viral hepatitis B.
- Familial HBV carriage was found in one patient.
- Two patients had a history of jaundice and one patient had a history of epistaxis.
- Two patients had known viral B cirrhosis.
- No patient was hypertensive or diabetic and no patient had known nephropathy.
- None of the patients were alcohol or tobacco consumers.

The most common circumstance of discovery was edema-ascitic syndrome associated with amenorrhea during pregnancy. It was associated or not with abdominopelvic pain, jaundice or digestive hemorrhage. In one case, the discovery was fortuitous in the presence of bicytopenia associated with gestational amenorrhea. Five patients had poor general condition. Two patients had infectious syndrome. Anemic syndrome was found in nine patients. Nine patients had edema-ascitic syndrome. One patient had cholestasis syndrome. PH syndrome was found in seven patients. Hepatomegaly was found in five patients. No patient had hepatic encephalopathy. No gynecologic-obstetric abnormalities were found in the patients.

Transaminases were elevated (hepatic cytolysis) in six patients. Prothrombin time was low in eight patients. Thrombocytopenia was found in nine patients. Anemia was noted in nine patients. Hyperbilirubinemia and hypoalbuminemia were found in nine patients. HBsAg was positive in eight patients and anti-HBc AC was positive in two patients. Analysis of ascitic fluid performed in three patients found two cases of ascitic fluid infection. Viral B DNA was performed in five patients and alpha-fetoprotein (AFP) in six patients. Anti-HCV AC and HIV serology were negative in patients who performed them. Abdominal ultrasound and pelvic or obstetric ultrasound were performed in all patients. Abdominal ultrasound revealed signs suggestive of a diagnosis of cirrhosis.

Pelvic or obstetric ultrasound showed a singleton pregnancy in all patients, including three pregnancies in the first trimester, three pregnancies in the second trimester and four pregnancies in the third trimester.

Upper digestive endoscopy performed on six patients found oesophageal varices in five patients. And only one patient had performed a Fibrometer which found severe F4 Fibrosis. No patient had performed an abdominal CT scan or a liver biopsy.

Cirrhosis was classified as Child A (compensated cirrhosis) in one patient;

Child B (decompensated cirrhosis) in one patient and classified as Child C (severe cirrhosis) in eight patients.

- *Maternal complications* that occurred were, nine cases of anemia and nine cases of ascites (**Table 1**) Two cases of digestive hemorrhage by rupture of oesophageal varices, Two cases of ascitic fluid infection, one case of conjunctival jaundice, one case of extensive portal thrombosis and two cases of hepatocellular carcinoma (HCC). One patient had no maternal complications.
- *Fetal and neonatal complications* that occurred included one case of fetal tachycardia; three cases of hypotrophy, one case of prematurity, one case of acute neonatal distress and two cases of fetal death in utero.
- *Favorable evolution*: four pregnancies had a favorable evolution without any complications.

Table 1. Maternal and neonatal complications occurred.

	Age (y)	Maternal complications	Fetal and/or neonatal complications
Obs 1	31	-Anemia -Ascites	-Acute neonatal distress -Hypotrophie
Obs 2	33	Any	Any
Obs 3	28	-Variceal bleeding -Anemia -Ascites	-Prematurity -Hypotrophy
Obs 4	26	-Variceal bleeding -Anemia -Ascites	Fetal death in utero
Obs 5	38	-Anemia -Ascites -Ascitic fluid infection	Any
Obs 6	34	-Conjunctival jaundice -Anemia -Ascites -Ascitic fluid infection	Hypotrophy
Obs 7	35	Anemia -Ascites	Fetal Tachycardia
Obs 8	30	-Anemia -Ascites	Any
Obs 9	30	-Anemia -Ascites -Extensive portal thrombosis -Hepatocellular carcinoma	Fetal death in utero
Obs 10	35	-Anemia -Ascites -Hepatocellular carcinoma	Any

4. Discussion

The mean age of patients at diagnosis was 32.5 years with extremes of 26 to 38 years. This result was close to that of Sermé [4] in Burkina Faso in 2016 who found a mean age of 32 years and higher than that of Itoudi [17] in Gabon in 2018 which found an average age of 26 ± 6 years. The young age of the patients could be explained by the mode of transmission of HBV in our context. Indeed, the main mode of contamination in areas of high endemicity such as Burkina Faso is perinatal transmission. This is either vertical transmission from mother to child during childbirth or transplacental when pregnant women have a high level of viral replication, or horizontal perinatal transmission between children when they are raised together.

All the patients were housewives. Eight patients resided in rural areas. Access to qualified medical personnel and adequate technical facilities was therefore difficult. Patients had to travel long distances to reach the city of Ouagadougou, which remains one of the localities in the country where certain specialized medical procedures are performed.

Indeed, over a period of 11 years, in a country with high endemicity of HBV infection such as Burkina Faso with a prevalence of 9.1%, we collected only 10 cases of cirrhosis and pregnancy out of a total number of 76,862 pregnancies. The rarity of this association in our country is consistent with literature data according to which the occurrence of pregnancy is a rare event in patients with cirrhosis, because cirrhosis is responsible for subfertility [16] [18]. The largest study reported is that of Whelton with 13 cases [3]. The association between cirrhosis and pregnancy was described in Africa and was rare [17], thus Dridi in Morocco reported one case [7]; Diarra in Mali reported one case [5]; N'Guéssan in Ivory Coast reported one case [6]; Ndubuda in Nigeria reported three cases [8] and Itoudi in Gabon reported 7 cases over a 3-year period [17].

None of our patients were vaccinated against HBV. This could be explained by a lack of information on the pathology and the high cost of the HBV vaccine. One patient was a carrier of HBsAg, two patients had known B viral cirrhosis and familial HBV carriage was found in one patient. This could be explained by the delay in screening in our context which is most often done at the disease or complication stage and especially by the insufficient awareness of HBV infection and its consequences in our country. Cirrhosis associated with pregnancy, although rare, is either discovered by chance or revealed by pregnancy due to the increased portal hypertension caused by pregnancy [19]. For the record, the association of cirrhosis and pregnancy probably goes back to the dawn of time; but the credit goes to Scaglione *et al.* [20] who in 1923 published the first case. In our study, cirrhosis was discovered in the presence of, either edemato-ascitic syndrome, abdominopelvic pain, jaundice, digestive hemorrhage or either bicytopenia associated to gestational amenorrhea. This could be explained by the delay in consultation, through the use of traditional treatments or self-medication, but also by the fact that cirrhosis remains asymptomatic for a long time and is only discovered when compli-

cations arise. The last circumstance of discovery reminds us of the importance of always thinking about it because of the hypersplenism that cirrhosis causes. Two patients had known and monitored B viral cirrhosis before the onset of their pregnancy. This shows that, although the occurrence of pregnancy is rare in patients with cirrhosis due to fertility problems caused by this pathology, pregnancy still remains possible [17] [21]. The poor general condition found in five of our patients could be explained by the therapeutic itinerary which lengthens the consultation time in our work context and especially the seriousness of the occurrence of a pregnancy in the cirrhotic patient [21].

The infectious syndrome was found in two patients. This indicates the presence of an infectious process. Indeed, infections are frequent during cirrhosis, especially bacterial ones, and would be the cause of an intercurrent infection, particularly pulmonary, urinary or repeated punctures, some of which do not respect the conditions of rigorous asepsis.

The most common clinical picture found in our patients was edema-ascitic syndrome found in nine patients; followed by portal hypertension (PH) syndrome found in seven patients. These data are consistent with those in the literature according to which the renal capacity to excrete sodium and free water during cirrhosis is impaired with hydrosodic retention and also, pregnancy which promotes an increase in portal pressures thus increasing the manifestations of PH complications [19] [22].

The elevation of transaminases is linked to chronic inflammation of the liver, thus leading to a release of its enzymes into the bloodstream. This indicates hepatic cytolysis generally accompanying cirrhosis or pre-existing chronic hepatitis. In addition, if the quotient of ASAT/ALAT is greater than 1 ($ASAT/ALAT = 2$), we have an indirect sign of cirrhosis.

Prothrombin time (PT) was decreased in eight patients in our study. This decrease in PT is biological evidence of IHC, thus revealing an advanced stage of the disease.

Thrombocytopenia was found in nine patients. The occurrence of this thrombocytopenia during cirrhosis has been described in the literature as being linked to hypersplenism. Portal hypertension then causes an accumulation and sequestration of all corpuscular elements of the blood, mainly thrombocytes in the hypertrophied and congested spleen [21] [22].

Hemoglobin level measurement revealed anemia in nine patients, but it could not be characterized due to the absence of MCV and MCHC values. This anemia is explained by an increase in blood loss due to acute or chronic digestive hemorrhages, dysfunction due to hepatitis viruses, and chronic inflammation.

The hyperbilirubinemia and hypoalbuminemia observed in our patients are related to the alteration of the synthesis and purification functions of the liver during cirrhosis.

Analysis of ascitic fluid in three of our patients revealed two cases of ascitic fluid infection. This could be explained by the frequency of bacterial infections at the

stage of decompensated cirrhosis due to the immunodeficiency which is multifactorial in these patients [23] [24].

Imaging: In terms of imaging, abdominal ultrasound performed on all our patients found signs suggestive of the diagnosis of cirrhosis, including hepatomegaly (six cases), nodular liver (four cases), heterogeneous liver parenchyma (seven cases), dysmorphic liver (five cases).

Extrahepatic ultrasound signs were associated, namely portal hypertension (ascites in nine cases, splenomegaly in four patients, dilatation of the portal trunk in two patients) and one case of portal thrombosis.

The obstetric ultrasound scan performed did not note any particular abnormality apart from fetal tachycardia found in one patient. It also made it possible to specify the gestational age and the number of fetuses. In fact, all the pregnancies were singleton, three women were in the first trimester, three women in the second trimester and four women in the third trimester of their pregnancy.

Upper Digestive Endoscopy (EDH) which was performed in six patients in our study found esophageal varices in five patients. They were grade III in three cases and grade II in two cases. Red signs were associated in four cases.

EDH did not find cardiopulmonary varices but found portal hypertensive gastropathy in four patients. These observed endoscopic signs are in line with literature data showing that increased portal blood flow and intrahepatic resistance cause increased pressure in the portal vein, leading to portal hypertension and subsequent formation of esophageal varices [18].

Abdominal CT scan was not performed in our patients probably because of its contraindication during pregnancy [25].

In principle, the diagnosis of cirrhosis is based on histological examination by liver biopsy. In practice, cirrhosis is accompanied by characteristic abnormalities that can be demonstrated by clinical examination, biological tests and imaging tests. Most often, the diagnosis of cirrhosis can be reasonably established without histological examination of the liver on the association of signs of PH and liver failure [26].

In our case, the liver biopsy puncture was not performed because of its contraindication in cases of thrombocytopenia.

Cirrhosis was classified as Child A (compensated cirrhosis) in one patient. It was classified as Child B (decompensated cirrhosis) in one patient and classified as Child.

C (severe cirrhosis) in eight patients. These different classes are stages of increasing severity of the pathology, thus reflecting the advanced stage of the disease in patients at the time of diagnosis.

All patients were HBV positive after performing hepatitis B serology. It then appears that the etiology of cirrhosis in our study was HBV. This observation is superposable to most of the results of African studies which give a large lead to the hepatitis B virus in the etiologies of cirrhosis in relation to a very high seroprevalence of the virus in the general population in Africa and more precisely in

our country where the carriage of the HBs antigen is high. In addition, no case of co-infection with the hepatic C virus or HIV had been noted.

In our study, two cases of digestive hemorrhage by RVO were noted. According to the literature, the main physiological modification during pregnancy is the alteration of the hemodynamic system which can aggravate portal hypertension and consequently the risk of hemorrhage by rupture of esophageal varices. According to Dridi [7], the main maternal complication remains digestive hemorrhage which requires urgent management and which is responsible for 50% of fetal mortality.

In our study, we noted nine cases of anemia. Sermé [4] in Burkina Faso had found four cases of anemia in their study. These cases of anemia could be explained by digestive hemorrhages but especially by hypersplenism found in cirrhosis.

For LALONDE [27], pregnancy in a cirrhotic woman involves many dangers, the most important of which are a possible terminal hepatic coma, possible digestive hemorrhages caused by the action of hypervolemia on the esophageal varices and the progressive worsening of

failure. The risk of hepatic coma increases with pregnancy due to the increase in estrogen which is toxic to the liver. Anemia is also a major complication with an incidence of 12.5% alongside toxemia (7% - 9%) in the evolution of cirrhosis during pregnancy.

Nine cases of ascites were noted in our study. Shaheen and Robert P. Myers [28] in a comparative study concluded that maternal complications such as ascitic decompensation, digestive hemorrhage by rupture of esophageal varices, hepatic encephalopathy, anemia... including maternal mortality in cirrhotic women and pregnant women are more frequent during the antenatal period than in the post-partum period.

Itoudi [17] in Gabon observed three maternal deaths in a hemorrhagic context in his study. On the other hand, in our study, we did not note any cases of hepatic coma or maternal death. We found two cases of ascitic fluid infection. This observation is similar to that of Sermé [4] who noted a case of ascitic fluid infection in his study. This could be explained by the high frequency of bacterial infections in cirrhotic patients. Indeed, ascitic fluid infection is a common complication during cirrhosis (representing 10 to 30% of bacterial infections in hospitalized patients) and associated with a poor prognosis [23] [29].

The jaundice presented by a patient in our study is a pejorative sign of the evolution of cirrhosis and could be linked to the alteration of the liver's purification functions during this pathology.

In our study, one case of portal thrombosis was noted. According to the literature, cirrhosis is no longer considered a hypocoagulable state; rather a risk (excluding hemorrhage related to portal hypertension) in cirrhosis, various clinical studies as well as a recent *in vitro* study support a thrombotic potential. The clinical findings of portal vein thrombosis in cirrhosis vary from asymptomatic disease to a life-threatening condition at first presentation. In the majority of patients

with cirrhosis, portal vein thrombosis is diagnosed on radiographic studies as an incidental finding, although in some patients, portal vein thrombosis may present as decompensation of their chronic liver disease. Its prevalence in cirrhotics is 10–25% and its 5-year incidence is of the order of 10% - 20% when portal vein thrombosis is systematically sought by Doppler ultrasound. Risk factors include severe disease (Child B or C cirrhosis), advanced age and a history of digestive hemorrhage due to rupture of esophagogastric varices [30] [31].

Two cases of probable HCC were reported in our study based on clinical and paraclinical arguments but were not confirmed. Indeed, hepatocellular carcinoma is the major complication of chronic liver diseases and particularly of cirrhosis whatever its etiology [32].

In our study, two cases of MFIU were noted and one case of premature delivery. This observation was close to that of Itoudi [17] in Gabon who found four cases of Intrauterine fetal death Fetal (IUFD) and one case of premature delivery.

Among the cases of IUFD, one occurred in a mother who had variceal bleeding. This finding is in line with the literature which supports that digestive hemorrhage is the main maternal complication requiring urgent management and which is responsible for 50% of fetal mortality. The abortion rate in cirrhotic parturients was 15 to 20%. Most cases of abortion are observed in the first trimester. According to Dridi [7], the main causes of pregnancy termination in the first trimester are spontaneous abortion in 18% to 20% of cases and therapeutic termination of pregnancy. During the second and third trimesters, digestive hemorrhage due to rupture of varices is the main cause of pregnancy termination. Perinatal mortality remains at a fairly high rate of 11% to 18%, mainly due to stillbirths, premature delivery in the second trimester, in utero growth retardation and neonatal death [33]. A case of abortion was noted in the study of Itoudi [17] unlike in our study where no case of abortion was noted. This could be explained by the small size of our sample but also by the uniqueness of our study center.

Four pregnancies were carried to term without fetal or neonatal complications. In the study by Itoudi [17], only one pregnancy was carried to term without incident. This observation is consistent with that of Moukit [34] who described a case of successful pregnancy in a cirrhotic patient.

5. Conclusion

This study confirmed that the association of cirrhosis and pregnancy is a rare phenomenon and constitutes a pregnancy with high risk of maternal, fetal and neonatal complications. Discovery of cirrhosis was fortuitous given clinical manifestations dominated by edema-ascitic syndrom in pregnant women. Biological manifestations were dominated by hepatocellular insufficiency syndrome. Abdominal ultrasound revealed signs suggestive of the diagnosis of cirrhosis and upper digestive endoscopy looked for signs of portal hypertension. The main etiology of cirrhosis was hepatitis B virus. Maternal complications were ascitic decompensation and anemia. Fetal and neonatal complications were dominated by

fetal hypotrophy and intrauterine fetal death. Nevertheless, four pregnancies were carried to term without any complications.

Management must be early and multidisciplinary, closely involving obstetricians, hepatologists and neonatologists. Although this study contributed to the understanding of this complex association, further research is needed to deepen the understanding of the pathophysiological mechanisms and to evaluate the effectiveness of preventive and therapeutic interventions.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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