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ORIGINAL ARTICLE

Pregnancy Outcomes in Patients with Early-Onset Idiopathic Chronic Pancreatitis

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Abstract

Background Early-onset idiopathic chronic pancreatitis (EOICP) is a disease that affects young individuals. Data on pregnancy outcomes in EOICP are limited.

Aim To assess the pregnancy outcomes in patients with EOICP and the effect of pregnancy on the course of EOICP.

Methods Patients with EOICP with disease onset before their pregnancy were recruited. Data regarding demographic variables, disease duration, pregnancy outcomes, and course of illness were noted.

Results 50 patients were included in the study contributing to a total of 86 pregnancies. The mean age of onset of symptoms and at the time of delivery was 17.95 (5.71) and 23.44 (4.28) years, respectively. Gestational diabetes (GD) and gestational hypertension (GH) noted in one (1.5%) each. 3 (4.5%) pregnancies were preterm. 19 (22.1%) pregnancies did not have successful outcomes (7 (8.1%) were induced abortions). 12 (15.2%) pregnancies had spontaneous pregnancy losses. 8 (10.1%) were spontaneous abortions and 4 (5.1%) were stillbirths. Of 67 successful pregnancies, 33 (49.3%) pregnancies were delivered by LSCS. Compared to average rates of LSCS in India, this was significantly higher (21.5% vs 49.3%—$p \leq 0.001$). The average birth weight was 2.87 (0.48) kg. There was one (1.5%) neonatal death. Compared to the published Indian data, there was no significant difference in the incidence of spontaneous pregnancy losses, GD, GH, preterm labor, and birth weight. Pancreatic pain was reported by 21 (42%) women in total 27 (31.4%) pregnancies. There was no difference in maternal or fetal outcomes between pregnancies with or without pancreatic pain. There were no pancreatitis-related complications reported during the pregnancies.

Conclusion The present study shows that mothers affected with EOICP have pregnancy outcomes similar to healthy women in India.

Keywords Chronic pancreatitis · Pancreatitis · Pregnancy · Idiopathic chronic pancreatitis · Maternal outcomes · Fetal outcomes

Introduction

Chronic pancreatitis (CP) is a progressive inflammatory disease leading to irreversible damage to the pancreas with resultant endocrine and exocrine insufficiency [1]. The prevalence of CP in India has been reported to be 125/100 000 population [2]. While alcohol is the most common cause of CP worldwide, in India, idiopathic CP accounts for 57.3%–69.6% of the cases of CP [3]. There are two variants of idiopathic CP. One with a disease onset less than 30 years (early-onset idiopathic chronic pancreatitis—EOICP) and the other with a later onset of the disease. EOICP is characterized by significant abdominal pain which impairs the quality of life [4].

The disease affects an individual in the prime of their lives. A dilemma in the minds of the young women afflicted with the disease is the effect the disease would have on the course of pregnancy. There are a paucity of literature on pregnancy outcomes in patients with EOICP. The present study was planned with the aim to study pregnancy

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outcomes in patients with EOICP and the effect of pregnancy on the course of CP.

Materials and Methods

Study Design

This was a single-center, observational study conducted at a large tertiary care center in South India. All women who visited the Pancreatic clinic between January 2014 and July 2022 and agreed to be included in a database of patients with EOICP were eligible for inclusion in this study. The inclusion criteria for the study were 1. Women more than 18 years of age, 2. Confirmed diagnosis of EOICP, and 3. Onset of disease prior to the pregnancy. Females with chronic pancreatitis due to other causes, as well as those with acute or recurrent acute pancreatitis, were excluded from the study.

Study Procedure and Data Collection

Patients were interviewed either in the Pancreatic clinic or telephonically and data regarding pregnancy was collected using structured questionnaires and review of delivery records. Data collection included demographic data, history, examination, laboratory, radiological, and endoscopic investigations, and prior medical, surgical, or endoscopic treatment details were noted. Details regarding symptoms during pregnancy, use of pancreatic enzyme replacement therapy (PERT), duration of pregnancy, mode of delivery, and outcomes of pregnancy were also noted.

Outcome Variables and Their Definitions

Clinical features (abdominal pain, steatorrhea, or diabetes mellitus) and imaging (CT scan /MRI scan/ultrasound/endoscopic ultrasound) findings of pancreatic ductal and/or parenchymal changes (calcification, atrophy, ductal dilatation) were used to diagnose chronic pancreatitis. Pancreatic exocrine insufficiency (PEI) was defined as fecal elastase levels < 200 µg/g. All the patients were evaluated for toxic (alcohol, smoking), metabolic, and structural risk factors for chronic pancreatitis. Patients who had disease onset at age ≤ 30 years and in whom no definite cause for chronic pancreatitis was identified were labeled as EOICP [5].

Preterm delivery It refers to a birth of a baby before 37 weeks of gestation [6].

Post-term delivery Post-term pregnancy refers to a pregnancy that has reached or extended beyond 42 0/7 weeks of gestation from the last menstrual period [7].

Abortion It refers to an early pregnancy loss before the 20th week of gestation or 139 days, counting from the first day of the last normal menses [8].

Stillbirth The term stillbirth refers to the delivery of a fetus at 20 weeks of gestation with no signs of life [9].

Spontaneous pregnancy losses Spontaneous abortion and stillbirth were considered spontaneous pregnancy losses.

Neonatal mortality It is defined as death occurring during the first four weeks after birth [10].

Low birth weight Low birth weight has been defined by WHO as a weight at birth of < 2500 g [11].

Gestational diabetes (GD) GD was defined as the onset or first recognition of abnormal glucose tolerance during pregnancy [12].

Gestational hypertension (GH) GH is defined as systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more on two occasions at least 4 h apart after 20 weeks of gestation in a woman with previously normal blood pressure in the absence of proteinuria or new signs of end-organ dysfunction [13].

Preeclampsia is a disorder of pregnancy associated with new-onset hypertension, which occurs most often after 20 weeks of gestation and frequently near term. Although often accompanied by new-onset proteinuria, hypertension and other signs or symptoms of preeclampsia may present in some women in the absence of proteinuria [13].

Eclampsia is the convulsive manifestation of the hypertensive disorders of pregnancy and is defined by new-onset tonic–clonic, focal, or multifocal seizures in the absence of other causative conditions, such as epilepsy, cerebral arterial ischemia, infarction, intracranial hemorrhage, or drug use [13].

Pancreatic pain Pancreatic pain was classified as type A and type B pain. Type A pain pattern, typically observed in acute relapsing pancreatitis, is short-lived pain episodes usually lasting < 10 days and separated by long pain-free intervals of several months to 1 year. Type B pain is characterized by prolonged periods of persistent (daily) pain and/or clusters of recurrent severe pain exacerbations [14].

The Izbicki score was calculated for each case. The Izbicki pain score is a validated pain score specifically designed for chronic pancreatitis. It consists of four questions regarding the frequency of pain, the intensity of the pain (VAS score), the use of analgesics, and disease-related inability to work. Based on these questions, a pain score can be calculated ranging from 0 (no pain) to 100 (severe, debilitating pain) [15].

Pancreatic exocrine insufficiency (PEI) PEI was defined by fecal elastase levels < 200 µg/g [16].

Outcome Measures

The primary objective of the study was to assess the outcomes of pregnancy in patients with EOICP. Preterm labor, GD, GH, eclampsia, preeclampsia, mode of delivery, and maternal death were listed as maternal outcomes.

Abortion, stillbirths, neonatal mortality, birth weight, and congenital abnormalities were all evaluated as fetal outcomes.

The secondary objective of the study was to assess the effect of pregnancy on the course of chronic pancreatitis. The course of chronic pancreatitis during pregnancy was noted in terms of pancreatic pain during pregnancy, steatorrhea, presence of diabetes, and other complications of chronic pancreatitis, like pseudocyst, vascular thrombosis, GI bleeding, biliary obstruction, duodenal obstruction, or pancreatic fistula (Fig. 1).

Statistical Analysis

The numerical data were expressed as mean ± SD and categorical variables as numbers and percentages. The difference between the two groups for continuous variables was compared using the Student's *t* test (for normal distribution)/Mann–Whitney test (non-normal distribution). The chi-square and Fisher's exact tests were used to compare categorical variables. All tests were two-sided at alpha = 0.05 level of significance. All the statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 21.0.

The study protocol was approved by the Institutional Review Board (IRB Min No. 13651).

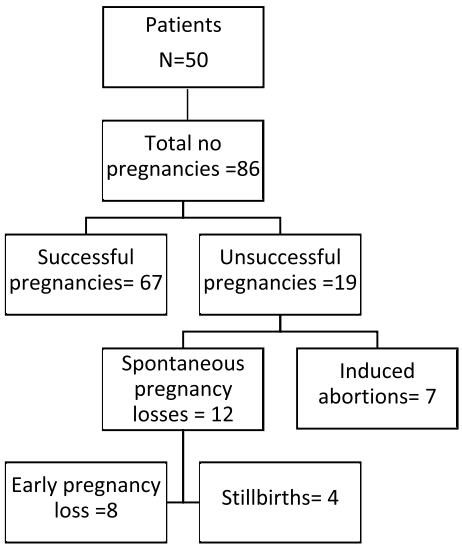

Fig. 1 Outcomes of pregnancies in patients with early-onset idiopathic chronic pancreatitis ($n = 50$)

Results

Study Population

Among the women with chronic pancreatitis who had visited the pancreatic clinic at CMC Vellore during the study period, 110 women with EOICP agreed to participate in a prospective database. Of the 110 women, 34 were unmarried, 10 were nullipara, 9 had disease onset after their pregnancy, and details regarding pregnancy were not available for 7 women. 50 women were included in the study group, contributing to 86 pregnancies. The baseline characteristics of the patients are provided in Table 1. The mean age of onset of symptoms was 17.95 (5.71) years and the mean age at diagnosis was 24.62 (6.28) years. 44 (88%) women had PEI, 5 (10%) had endocrine insufficiency, and 44 (88%) had calcifications.

Table 1 Clinical characteristics of patient with early-onset idiopathic chronic pancreatitis at presentation ($n = 50$)

Parameter	Value
Age of onset of the disease (years) Mean (SD)	17.95 (5.71)
Age at the time of diagnosis (years) Mean (SD)	24.62 (6.28)
Addictions *n* (%)	
Alcohol	0 (0)
Smoking	0 (0)
Imaging findings *n* (%)	
Pancreatic calcifications	44 (88)
Pancreatic parenchymal atrophy	42 (84)
Main Pancreatic duct dilatation	44 (88)
Females with complications of chronic pancreatitis *n* (%)	
Pancreatic exocrine insufficiency	44 (88)
Pancreatic diabetes	5 (10)
Pseudocyst	0 (0)
Vascular thrombosis	0 (0)
GI bleeding	0 (0)
Biliary obstruction	0 (0)
Duodenal obstruction	0 (0)
Pancreatic fistula	0 (0)
Patients on pancreatic enzyme replacement therapy during pregnancy *n* (%)	5 (10)
Surgery for pancreatic pain *n* (%)	4 (8)
Pancreatic endotherapy for pain management *n* (%)	4 (8)
Extracorporeal shockwave lithotripsy *n* (%)	1 (2)
Pancreatic stenting *n* (%)	3 (6)
Age at the time of delivery (years) Mean (SD)	23.44 (4.28)

Pregnancy Outcomes in EOICP

The majority of the pregnancies (43%) were Primigravida. The mean age at the time of delivery was 23.44 (4.28) years. GD and GH were noted in one (1.5%) each. Preeclampsia or eclampsia was not noted in the study group. The majority of the deliveries were term deliveries; however, 3 (4.5%) deliveries were preterm. There was no maternal demise.

19 (22.1%) pregnancies did not have successful outcomes, of them 7 (8.1%) were induced abortions. 12 (15.2%) pregnancies had spontaneous pregnancy losses. Among them, 8 (10.1%) were spontaneous abortions and 4 (5.1%) were stillbirths. Among these 19 patients with unsuccessful pregnancy outcomes, three patients had pancreatic pain during pregnancy. The cause for spontaneous or induced abortions was obstetric and not secondary to pancreatic pain. Of 67 successful pregnancies, 33 (49.3%) pregnancies were delivered by Lower Segment Cesarean Section (LSCS). Compared to average rates of LSCS in India, this was significantly higher (21.5% vs 49.3%—$p = < 0.001$) [17]. The average birth weight was 2.87 (0.48) kg. Five babies had low birth weight and one had macrosomia. There was one (1.5%) neonatal death. We compared our study outcomes with the existing database of pregnancy outcomes of healthy Indian females—Table 2. There was no significant difference in the incidence of spontaneous pregnancy losses, GD, GH, preterm labor, or birth weight [18–22]. Five (10%) of the patients reported the use of PERT during pregnancy. However, there were no congenital anomalies reported in the study population.

Course of Chronic Pancreatitis During Pregnancy

Pancreatic pain was reported by 21 (42%) women in a total of 27 (31.4%) pregnancies. The mean Izbicki pain score was 29.88 (23.26). Most of the women (66.7%) had type A pancreatic pain and 52.4% of patients required hospitalizations for pain management. Majority of patients reported the use of non-opioid analgesia, and opioid analgesia was used in two pregnancies with severe pancreatic pain. When we compared the pregnancy outcomes between patients without pancreatic pain and those with pancreatic pain, we found no difference in maternal or fetal outcomes—Table 3. Steatorrhea was reported by one patient (2%), whereas diabetes was noted in 5 (10%) patients. No chronic pancreatitis-related complications (pseudocyst, vascular thrombosis, GI bleeding, biliary obstruction, duodenal obstruction, or pancreatic fistula) were reported during the pregnancies.

Discussion

Pregnancy induces physiological changes within a woman which allow the mother to nurture and deliver a healthy baby. Healthy women tolerate the consequences of these physiological changes; however, women with an underlying

Table 2 Comparison with published data from India

Parameter	Published data study name	Published data values	Study population	*p* value
Gestational diabetes %	Swaminathan et al. [19]	1.3	1.5	0.89
Gestational hypertension %	National Health Portal Of India [20]	7.8	1.5	0.05
Spontaneous pregnancy losses %	Maharana et al. [18]	10	15.2	0.124
Preterm %	Tellapragada et al. [21]	7.6	4.5	0.335
LSCS %	National Family Health Survey 5 [17]	21.5	49.3	0.001
Mean birth weight (kg) mean (SD)	Kumar et al. [22]	2.91 (0.57)	2.87 (0.48)	0.0928
Low birth weight %	Tellapragada et al. [21]	11.4	7.5	0.302

LSCS Lower Segment Cesarean Section

Table 3 Comparison between patients without pancreatic pain and with pancreatic pain

Parameter	Patients without pain	Patients with pain	*p* value
Gestational diabetes *n* (%)	0 (0)	1 (100)	0.343
Gestational hypertension *n* (%)	1 (100)	0 (0)	1.000
Spontaneous pregnancy losses *n* (%)	8 (66.7)	4 (33.3)	1.000
Preterm *n* (%)	2 (66.7)	1 (33.3)	1.000
LSCS *n* (%)	24 (72.7)	9 (27.3)	0.231
Mean birth weight (kg) mean (SD)	2.88 (0.54)	2.86 (0.37)	0.917
Low birth weight *n* (%)	4 (80)	1 (20)	1.000

LSCS Lower Segment Cesarean Section

co-morbid condition may respond variably to these changes. EOICP is a unique subset of chronic pancreatitis in which the disease afflicts young individuals. Young women afflicted with the disease frequently question the implications of the disease on pregnancy outcomes. Therefore, we planned this study to understand the outcome of pregnancy in patients with EOICP and the clinical course of chronic pancreatitis during pregnancy.

The women included in the study had disease onset prior to their pregnancy and a majority of the women had advanced disease with pancreatic calcifications and exocrine insufficiency noted in 88% of the individuals. Despite the advanced disease, a majority of the patients had a successful full-term pregnancy. No major obstetric complications were noted. We compared the obstetric outcomes with published results in healthy Indian women—Table 2. The rates of GD, GH, spontaneous pregnancy losses, and preterm labor in the study population were similar to those in healthy women. The mean birth weight of the children was comparable to the national average. Although the results are comparable to published literature, it may not be truly reflective due to the small sample size of our study. The mean rate of LSCS in the study population (49.3%) was significantly higher than in the national database (21.5) ($p = 0.001$). The reason for the high LSCS in this group of individuals is unclear. Maternal comorbidity may have been a determining factor contributing to physicians' preference for cesarean section in this group [23]. The incidence of preterm labor was 4.5%, this was similar to what has been reported by Mahapatra et al. in their study on women with chronic pancreatitis [24]. When compared to Tellapragada et al., the incidence of preterm labor was similar to that in healthy Indian women [21].

One major concern of expectant mothers is pancreatic pain during pregnancy. Approximately, 40% of the patients experienced pancreatic type of pain during pregnancy. Although half of them required hospitalization, most of the pain episodes could be managed with analgesics alone. Most of the patients had type A pain. We compared the pregnancy outcomes in patients with and without abdominal pain. There was no difference in the incidence of obstetric complications viz, GD, GH, spontaneous pregnancy losses, or preterm labor between the two groups. Many immune-mediated diseases, such as uveitis, and multiple sclerosis improve during pregnancy [25–27]. We did not notice any similar change in the disease course of patients with chronic pancreatitis; however, the incidence of pancreatitis-related local complications was lower in the study population.

Although a majority of women had PEI, only 10% were on regular PERT during pregnancy. Currently, there is lack of clarity on the safety of PERT during pregnancy. PERT has been included as a schedule C drug as per Food and Drug Administration in pregnant women [28, 29]. The number of patients on PERT in this study was very low and therefore we could not determine the safety of PERT during pregnancy. In a similar study, patients were on PERT during pregnancy and the authors felt that PERT during pregnancy is probably safe [24]. A study with a larger number of patients on PERT may be able to give a better answer as regards the safety of PERT. Our study showed that the majority of the patients with EOICP had successful pregnancy outcomes and the course of chronic pancreatitis was benign. Also, there were no complications of chronic pancreatitis noted during pregnancy.

In a similar study on pregnancy outcomes in patients with chronic pancreatitis, Mahapatra et al. found no evidence of adverse maternal or fetal outcomes [24]. Our findings are consistent with those of this study.

The strength of our study is this is the first study to assess the pregnancy outcomes in a special subgroup population of EOICP. We acknowledge certain limitations of our study. Owing to the nature of the study, there is a possibility of recall bias. Also, details regarding the pre- and post-pregnancy course of illness were not available. Therefore, the trend in the symptoms could not be assessed.

To conclude the present study shows that mothers affected with EOICP have pregnancy outcomes similar to healthy women in India.

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Author's contribution Guarantor of the article: SDC. Study concept and design: SDC and SB. Acquisition of data—GK and SDC. Analysis and interpretation of data—SDC, RTK, AT, and AKD. Critical revision of the manuscript for intellectual content: SDC, EGS, and AJJ. Final approval of the manuscript: SDC.

Declarations

Conflict of interest The authors declare no conflicts of interest regarding this article.

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