

# Acute Fatty Liver of Pregnancy: A Clinical-Paraclinical Survey

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**Background:** Acute Fatty Liver of Pregnancy (AFLP) is one of the serious complications of the pregnancy period. Surveying the laboratory and clinical signs is effective in timely prognosis and fast treatment of this illness.

**Objectives:** The current study aimed to evaluate AFLP among the hospitalized subjects.

**Patients and Methods:** This retrospective study was conducted on clinical and preclinical records of 25 females with AFLP for maternal and perinatal prognosis from 2000 to 2009. The data was analyzed using SPSS ver. 19.

**Results:** The patients aged 16 - 45 years old with one to four pregnancies; they were 24 to 39 weeks pregnant with the mean of 33.56 weeks, and 56% were multifariorous. The most prevalent clinical symptoms were nausea, vomiting, abdominal pain, headache, pruritus, and icterus. The laboratory signs included disorders of liver, coagulation, kidney, and hypoglycemia. Nausea and vomiting in the first and second age groups (Group 1, patients were < 25 years; Group 2, patients were 25 - 35 years) and abdominal pain (100%) in the third group (Group 3, patients were > 35 years.) were the most prevalent symptoms. No patient had fever, ascites, and polydipsia. There was one case of mother and fetal death.

**Conclusions:** In the current study, the clinical and paraclinical signs of AFLP were mostly - liver, coagulation, kidney, and hypoglycemia disorders. Considering that patients mostly refer in three phases of clinical, laboratory, and complications, it is essential to evaluate the suspected ones who present clinical symptoms especially nausea, vomiting and abdominal pain.

**Keywords:** Fatty Liver; Pregnancy; Prognosis

## 1. Background

Acute Fatty Liver of Pregnancy (AFLP) is a rare complication, which tends to manifest in the first pregnancies in subjects aged below 25. AFLP occurs more often in the pregnancies with a male fetus (75%) (1, 2), and is more prevalent in nulliparous subjects (3, 4). The incidence of AFLP is from one in 10,000 to one in 16,000. Its maternal and fetal mortality rates are 18% and 23%, respectively (3). For the first time, it was described with hepatic microvascular statuses in 1940 (5). No ethnic and regional varieties and diseases of pregnancy period affect the occurrence of this disease. In addition, AFLP may not be apparent in the immature girls and menopause females (4). The exact etiology of AFLP is unknown; however, considering physiopathological matters, the most important factor for AFLP is a mitochondrial disorder in the fatty acids oxidation and their accumulation in the hepatocytes. Penetration of fatty acids causes acute hepatic failure if not diagnosed or treated early; consequently, it will cause irreparable complications such as maternal or neonatal death (4), cardiomyopathy, neuropathy, myopathy, non-ketonic hypoglycemia, hepatic failure, and asphyxia (6). Although its cause is unknown, the viral, dietary, and poisoning reasons may be suspected (1, 2). Placenta plays an

important role in this disease, because of the post-delivery observation, the liver function returns to its normal condition (4, 7, 8). Oxidation of fatty acids is normal in females with AFLP; however, in pathologic conditions, the embryo is not able to oxidize the fatty acids (1, 2), and by transferring them to mother, while the mother cannot metabolize the extra fatty acids, it leads to AFLP. The differential diagnosis is in the third trimester of pregnancy (9). Clinical signs usually begin from the second trimester (2) and aggravate in the third trimester (10, 11). Moreover, the most prevalent signs are nausea and vomiting in 70% and 75% of the subjects, respectively (6, 12). Abdominal pain (50% - 80%), tenderness in the right upper quadrant (2, 13), fever, headache, backache, reflux, diarrhea, gastrointestinal bleeding, hypertension, jaundice, acute tubular necrosis, hepatorenal syndrome (14), pancreatitis, reduction of the liver size, hepatoencephalopathy, ascites (50%), coma, and reduction in the level of consciousness are the other mentioned clinical symptoms (2). Compared to the past, maternal mortality has decreased because of the improvement in diagnosis and the supportive actions (6, 15, 16) from 90% to 20% (8, 17). The previous studies showed that plasma exchange espe-

cially in severe cases, leads to remission of the laboratory signs and indices (18). Although the patients recover after labor, their laboratory indices remain abnormal for a period and rarely progress to hepatic failure and liver transplantation (19). Temmerman et al. (11) reported the prevalence of laboratory abnormalities about 3% to 5%. Since the rise in some blood markers were used in the diagnosis of fatty liver, the prognosis of laboratory disorders in females with AFLP was effective in the treatment and reduction of the complications of the mother and the embryo (3, 20). These laboratory abnormalities include hypoglycemia, hyperbilirubinemia (1, 20), increase of the hepatic enzymes (1, 20), alkaline phosphatase (1, 20), kreatinin, uric acid, metabolic disorders (21), lactic acidosis, reduction of coagulation factors (22), an increase in the prothrombin time (PT) (20), low fibrinogen, and antithrombin (22). Other laboratory abnormalities are reduction of platelet life, leukocytosis, neutrophilia, thrombocytopenia, normoblasts, giant platelet, basophilic stippling, and break down of red blood cells (1). Besides, determination of the most basic clinical and in vitro results of AFLP in females, proper analysis of the liver function test (LFT), and recognition of different clinical and laboratory abnormalities in early phases (9) can affect the proper care and reduction of the illness complications (20, 23, 24).

## 2. Objectives

The current study aimed to survey the demographic characteristics, and clinical and laboratory signs of females with AFLP in Imam Khomeini and Razi hospitals of Ahvaz, Iran, from 2000 to 2009.

## 3. Patients and Methods

In the current retrospective study, the medical records of 25 females with AFLP from Imam Khomeini and Razi hospitals of Ahvaz from 2000 to 2009 were reviewed. The Ethic Committee of the Ahvaz Jundishapur University of Medical Sciences approved this study and all the patients signed the informed consent letters. A questionnaire, including demographic characteristics, clinical, and laboratory findings (symptoms and signs) was arranged, and the data of the records were gathered. The questionnaire was designed according to the opinions of a number of socio-medical experts, gynecologists, and based on the context validity by the referral to the similar studies. The patients were divided into three age groups < 25, 25-35, and > 35 years.

### 3.1. Statistical Analysis

The data were analyzed using SPSS version 19.0. The qualitative variables were presented as percentage; and the quantitative variables were described by mean and SD. Chi-square and T-tests were used to analyze the results and P-values less than 0.05 were considered as significant.

## 4. Results

The study surveyed the clinical and paraclinical signs of AFLP (Tables 1 and 2). The patients in the study aged 16 - 45 years (mean: 27.2 ± 7.05). Eight patients were < 25 (32%), 14 were 25 - 35 (56%) and three were > 35 (12%) with one to four pregnancies (mean: 1.96 ± 1.02). They were 24 to 39 weeks pregnant with the mean of 33.56 weeks. One patient was between 14 and 27 weeks pregnant with the mean (4%) and the rest were over 27 weeks (96%). Eleven patients were nulliparous (44%) and 14 patients were multiparous (56%). Six subjects experienced the second pregnancy (24%), six patients experienced the third (24%) and two persons experienced more than three pregnancies (12%). The clinical symptoms were nausea and vomiting, abdominal pain, headache, pruritus, and icterus, in 44%, 36%, 20%, 16%, and 8% of the subjects, respectively (Table 1). Symptom observations were as follows: In the first age group nausea and vomiting 27.5%, abdominal pain 25%, headache 12.5%; in the group aged 25 - 35 years nausea and vomiting 50%, abdominal pain and headache 28.6%; and in the group aged over 35 abdominal pain 100%, nausea and vomiting 33%.

No patient had fever, ascites, and polydipsia. The frequency of paraclinical signs were as follows: hyperbilirubinemia 44%, increase in prothrombin time 32%, thrombocytopenia 24%, hypoglycemia and increase of alkaline phosphatase and kreatinin each 20%, prothrombin activity 16%, increase of albumin 12%, increase of partial thromboplastin time (PTT), leukocytosis 8%, and neutrophilia and uric acid increase 4% (Table 2). Only a 39-year-old mother died with fetal death. Her clinical and paraclinical signs included abdominal pain, leukocytosis, thrombocytopenia, increase in alkaline phosphatase and kreatinin, coagulation disorder, and increase in bilirubin. Also 64% of the females had (medical) illness. In the current study hyperbilirubinemia (P = 0.010), hypoglycemia (P = 0.005), and pruritus (P = 0.014) were significant in nulliparous females.

**Table 1.** The Clinical Signs of Acute Fatty Liver of Pregnancy According to the Age (n = 25)<sup>a, b</sup>

Clinical Signs	Group 1	Group 2	Group 3	Total, %
Nausea and vomiting	3	7	1	44
Abdominal pain	2	4	3	36
Headache	1	4	0	20
Pruritus	2	2	0	16
Icterus	1	1	0	8
Impatience	0	1	0	4
Lethargy	0	1	0	4
Fatigue	0	1	0	4
Polyuria	1	0	0	4

<sup>a</sup> Group 1, patients were < 25 years; Group 2, patients were 25 - 35 years; Group 3, patients were > 35 years.

<sup>b</sup> Data are presented as No.

**Table 2.** Laboratory Signs According to Age (n = 25) <sup>a, b</sup>

Laboratory Signs	Group 1	Group 2	Group 3	Total, %
Hyperbilirubinemia	3	6	2	44
prothrombin time	2	4	2	32
Thrombocytopenia	2	3	1	24
Alkaline phosphatase	1	3	1	20
Kreatinin	2	2	1	20
Hypoglycemia	3	1	1	20
Prothrombin activity	0	2	2	16
Albumin	1	2	0	12
Partial prothrombin time	0	0	2	8
Leukocytosis	1	0	1	8
Neutrophilia	1	0	0	4
Uric acid	1	0	0	4

<sup>a</sup> Group 1, patients were < 25 years; Group 2, patients were 25 - 35 years; Group 3, patients were > 35 years.

<sup>b</sup> Data are presented as No.

## 5. Discussion

Acute Fatty Liver of Pregnancy is a pathological process related to pregnancy period without known reasons and a wide spectrum of clinical and laboratory signs (24). It sometimes becomes so serious that needs medical intervention. All the physicians, gynecologists, and healthcare providers may need to survey the clinical and laboratory signs before labor. Moreover, after observing the suspicious signs, proper surveys should be conducted for the accurate diagnosis. In the current study nausea, vomiting, abdominal pain, headache, pruritus and icterus were the most prevalent clinical signs, respectively. These signs were more prevalent in the group aged 25 - 35, compared to the other two groups, probably due to the difference in the number of subjects in the groups. In most of the similar studies, such as the ones by Fesenmeier et al. (6), Vigil-de Gracia et al. (12), and Ch'ng et al. (23), nausea and vomiting were the most prevalent clinical signs, which were similar to the current study. It seems that due to the difference between samples results of this study with Fesenmeier, studies (6).

Early diagnosis of this disease is of great importance because of the differential diagnosis with gastrointestinal signs in the second and third trimester of pregnancy; healthcare providers should consider this point during the examination of pregnant women. The current study was retrospective and the study by Ch'ng et al. (23) was prospective; however, the abdominal pain was the second most prevalent sign in the two studies. In the current study, the frequency of abdominal pain rose as age increased; 100% of the subjects over 35 years had abdominal pain. The obtained result shows the importance of this sign compared to other clinical signs in this age group. Surveying this result more by bigger sample size in a

prospective study is recommended. In the current study, there were laboratory abnormalities such as liver, kidney, and coagulation disorders, and hyperglycemia in order of prevalence, which were similar to the study of Lau (24); nevertheless, Vigil-de Gracia (12) reported kidney, liver, and coagulation disorders, and also hypoglycemia. To survey this difference, a bigger study with more sample size is necessary. In the current study, comparing all multiparous (56%) with nulliparous subjects (44%), the multiparous ones were more frequently affected by the AFLD. However, compared to multiparous subjects, AFLP was more prevalent among nulliparous ones. Although the type and sample size of the current study were different from those of Lau et al. (24) and Fesenmeier et al. (6), the results were consistent. AFLP seems to be mostly related to the number of pregnancies. In addition, the most prevalent laboratory signs were the same in multiparous and nulliparous groups. Besides, the most common clinical symptom in the nulliparous subjects was pruritus, and in multiparous ones were nausea, vomiting and abdominal pain. In the present study, the disease was prevalent among 25 - 35 years old subjects, but in the studies by Lau et al. (24) and Fesenmeier et al. (6), it was prevalent in the group under 25, and the difference was probably due to the prevalence of pregnancy under 25 years from 1999 to 1992. The current study showed that the clinical signs begin from the second trimester and aggravate in the third trimester of pregnancy; but Ko HH et al. (9) believe that the signs appear in the third trimester or in the beginning of the pregnancy. It seems that this disease appears from late second trimester to the beginning of the post labor period. In the current study, there was one case of neonate and mother's death. In the study by Fesenmeier (6), there were two cases of mothers' death and three cases of embryos' death. Since the signs of the disease are unspecific, the mortality is probably due to not timely diagnosis of the disease. It is tried to diagnose AFLP in women referring to clinics, paraclinics, during the clinical and complication phases. Routine laboratory evaluation revealed that hyperbilirubinemia moderately elevated liver transaminase, but the results for hepatitis virus testing were negative. Awareness of therapeutic attendants and accurate diagnosis of pregnant women with the suspected clinical symptoms especially nausea, vomiting and abdominal pain from the late second trimester to the beginning of the post labor period is suggested to prevent the dangerous complications of the disease.

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