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RESEARCH ARTICLE

PREDICTORS OF POOR PROGNOSIS IN PREGNANT WOMEN WITH COVID-19: A PROSPECTIVE COHORT STUDY IN THE MATERNITY MOTHER AND CHILD UNIVERSITY HOSPITAL OF CASABLANCA MOROCCO

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Abstract

Objective: We aim to study the clinical characteristics, the evolution of COVID-19 on pregnant women and survival factors.

Study design: It's a prospective cohort study in a large tertiary maternity unit within the Mother and Child University Hospital Ibn Rochd of Casablanca with an average annual birth of over 6950 births. We prospectively collected and analyzed data for a cohort of 40 pregnant patients tested positive for COVID-19 between January 2020 and December 2020 inclusive to assess the effect of COVID-19 on pregnancy.

Results: Forty pregnant patients tested positive for COVID-19, 36 patients gave birth and 4 patients died pregnant. The severity of the symptoms ranged from mild in 20/40 (50%) of the patients, moderate in 7/40 (17,5%), and severe in 13/40 (32,5%). Thirteen of our patients were admitted to intensive care units, six were in their third trimester, and seven in their second trimester; nine were intubated and ventilated prior to delivery and three of them required Extracorporeal membrane oxygenation. Among these patients intubated only two survived. Most common comorbidities were gestational diabetes 4/40 (10 %), asthma 4/40 (10 %), preeclampsia 7/40 (17,5%). Of the 40 pregnant patients 31 (77,5%) were in their third trimester, 8 (20%) women in their second trimester, and one in her first trimester. Of the 36 patients who delivered, 12/36 (33,3 %) were preterm delivered by elective C-sections. The death rate was 17,5% (7/40).

Conclusion: COVID-19 is associated with high prevalence of preterm birth, caesarean section, and a high mortality rate.

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Introduction:-

December 2019 was marked by the emergence of a new coronavirus [SARS-CoV-2] which appeared in China, responsible for an epidemic (COVID-19) that has spread across the world [1]. Currently the number of cases continues to increase worldwide. In Morocco, the first case was detected on the 2nd of March 2020, bringing the situation on the 31st of December 2020 to 439 193 cumulative cases since the start of the pandemic, with 407 504 healings and 7 388 deaths [2]. Pregnant women especially are particularly at risk of severe complications regarding COVID-19 infections, due to the possible physiological changes associated with pregnancy as well as the clinical manifestations of the disease [3,4]. Data from SARS-CoV, indicate that infection in pregnancy tends to be severe and associated with adverse neonatal outcomes, including increased risk of miscarriage, fetal growth restriction, and preterm birth while the risk of vertical transmission is inconclusive [5-8]. The identification of the clinical, biological and radiological manifestations, the risk factors and complications of the COVID-19 as well as their evolutions are essential to the management of maternal-fetal care. The aim of this study is to describe the symptoms and outcomes in infected pregnant women of SARS-CoV-2 in a tertiary maternity unit within the University Hospital of Casablanca in Morocco a developing country.

Materials and Methods:-

It's a prospective clinical study, the information was collected while the patients were hospitalized from January 2020 to December 2020 inclusive and analyzed using SPSS software. For each patient, a proforma was attached to the clinical note which was completed at each stage of the hospital stay. Telephone follow-up of maternal recovery were carried out by the doctors and was added to the medical file. The qualitative parameters were expressed as an absolute value and the quantitative parameters as a percentage. All patients were willing to explore their charts. The infection was confirmed based on positive Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) results on maternal nasopharyngeal samples. All women were followed in the maternity ward until childbirth.

Results:-

A total of 6950 pregnant patients were admitted in our Maternity, of which 73 had suspected COVID-19 symptoms for which nasopharyngeal samples for RT-PCR for SARS-CoV-2 nucleic acid were taken. 40/73 (54,8%) of patients had confirmed COVID-19 infection based on the RT-PCT test (figure 1). Most patients 32/40 (80%) had a respiratory symptoms (including 13 severe), 7/40 had a digestive symptom and 19/40 had flu syndrome.

Mean age of patients was 31,1 [18;40] years, 13/40 (32,5%) were admitted to intensive care unit (ICU), 9/40 (22,5%) required mechanical ventilation, and 3/40 (7,5%) required extracorporeal membrane oxygenation (ECMO). Comorbidities were gestational diabetes 4/40 (10%), Asthma 4/40 (10 %), preeclampsia 7/40 (17,5 %). One pregnant woman had hypertension, one had a mitral valve replacement, two had well-controlled hypothyroidism, one had hepatitis B and Retinitis pigmentosa, and one patient had pulmonary tuberculosis.

In our cohort of 40 women, we had 31 (77,5%) pregnant women with confirmed COVID-19 in their 3rd trimester, 8 (20%) women with confirmed COVID-19 in their second trimester, and one in her first trimester. The gestation at delivery varied from 17 weeks of amenorrhea to 40 weeks. Of the 36 patients who delivered, 12/36 (33,3%) were preterm.

The majority had caesarean deliveries 23/36 (63,8%). 20/23 (86,9%) had an emergency C-sections while 3/23 (13%) had an elective C-section. Indications for the emergency C-sections included fetal distress 10/23 (34,7%), development of maternal severe adult respiratory distress syndrome 6/23 (26%), third trimester hemorrhages 3/23 (13%) one had a complete placenta praevia, the second one had a placenta accreta for which she had a hysterectomy, the third one had a retroplacental hematoma and one had a severe preeclampsia and 3 elective C-sections, for primiparous site and a bicatricial uterus (Table 1).

Thirteen of our patients were admitted to ICU, nine were in their third trimester, and five in their second trimester. Nine were intubated and ventilated prior to delivery and two of them required ECMO. Among these patients (intubated) only two survived, the first was a woman of 29 years old who was in her third trimester, with well-controlled asthma, she was admitted in the maternity with mild symptoms (cough and dyspnea) and an oxygen saturation of 92%, we did a test PCR which was positive. The evolution was marked by a respiratory distress, she

delivered by C-section and was then admitted in the ICU with an oxygen saturation of 73%, where we did a CT scan revealing pulmonary lesions extended to 15% of the lungs, with a good evolution under standard treatment.

and was discharged after 14 days. the second patient was a woman of 34 years old who was in her third trimester, she had an emergency C-sections for development of maternal severe adult respiratory distress syndrome, with a CT scan revealing pulmonary lesions extended to 75% of the lungs. she was intubated and ventilated for 20 days and stayed at the ICU for 33 days where presented paraparesis with cerebral left frontal hematoma (non-surgical) on CT scan and perilesional edema and press syndrome on cerebral MRI then she developed an intensive care neuromyopathy for which she is followed in the neurology department.

In our cohort, we had seven maternal deaths, their age varied from 23 to 40 years old, five were in their second trimester and two in their third trimester; the gestational age varied from 19 weeks and four days to 40 weeks of amenorrhea. Among these patients, two had a gestational diabetes, one had preeclampsia, a patient had asthma, another patient had pulmonary tuberculosis, and one patient was suspected of having a systemic lupus erythematosus concomitant to the COVID-19 infection. Among our patients, three were admitted directly in the ICU, with severe respiratory symptoms. One of these three patients was 24 years old, she had pulmonary TB, and had ceased treatment on her own, she had a twin pregnancy at approximately 6 months, she was admitted in shock after a massive hemoptysis, and had a miscarriage. She died the following day after all resuscitation measures were taken. The second patient was 40 years old; she was 5 months pregnant, had gestational diabetes and preeclampsia and was admitted in the ICU with severe respiratory distress, she was immediately intubated and ventilated, and put on ECMO, initially her laboratory analysis was normal, it evolved towards a hemolysis elevated liver enzymes and low platelet syndrome (HELLP) and disseminated intravascular coagulation (DIC) and died 20 days after her admission from septic shock while still pregnant. The third patient was 23 years old; she was 20 weeks and 5 days pregnant, admitted with fever and icterus which appeared a week before her admission. At her admission she was hemodynamically, respiratory, and neurologically stable, but with biological anomalies evoking a hepatitis. She then deteriorated neurologically and was intubated and ventilated, the termination of pregnancy was indicated (the neonates were delivered by C-sections, in apparent death, 2/10 Apgar). An MRI showed encephalopathy lesions, the etiological investigations objectified a SLE, combining hepatic and neurological damage, concomitant with the COVID-19, the patient was declared brain dead, 25 days after her hospitalization. The four other patients were first admitted to the maternity with moderate symptoms and evolved to a severe respiratory state which lead to their transfer to the ICU where they were all intubated and ventilated, their age varied from 28 to 40 years old, only one patient had a well-controlled diabetes, with no other comorbidities. Two of the patients had a CT-scan revealing frosting glass scan lesions in favor of COVID-19, extend to 40% of the lungs for one patient and 60% for the second patient. Among these four patients, two underwent C-sections for development of maternal severe adult respiratory distress syndrome, one patient had a miscarriage, and the last one died before childbirth. The causes of death were respiratory arrest due to lung parenchyma destruction. The length of hospitalization varied from one day to 26 days.

In unified analysis (table 2) (figure 1-4) the probability of survival at day 12 of hospitalization is reduced to almost 50% in the event of flu syndrome ($p=0.039$), survival is almost 60% in lymphopenic patients ($p=0.012$), in cases of elevation of the D-dimers ($p=0.007$) and in patients who have used ECMO ($p=0.007$).

Table 1:- Clinical data and follow-up data of 40 cases of pregnant women infected with COVID-19, in the Maternity of University hospital Ibn Rochd, Casablanca.

Clinical Features (40 pregnancies)	
Maternal age (years)	Varies from 18 to 40 years with mean of 31,1 years
Comorbidities (13 pregnancies)	Gestational diabetes (4), Asthma (4), HTN (7), Cardiopathy (Mitral valve replacement) (1), Hypothyroidism (2), Hepatitis B (1), Retinitis pigmentosa (1), Pulmonary tuberculosis (1)
Signs and symptoms	
Antenatal Pyrexia	20 patients
Postpartum Pyrexia	02 patients
Shortness of breath, chest pain	12 patients
Dry cough	32patients
Diarrhea, abdominal pain	7 patients
Chest CT scan evidence of 2019-nCoV pneumonia (16 patients)	Chest CT positive in 14 patients

Delivery process (36 patients) Gestation at delivery Delivery Method Indication for C-section	24 patients were full-term, 12 were pre-term, C-sections (23 patients), normal vaginal delivery (13 patients) 3 elective C-sections, 20 EMCS Fetal distress (10), development of maternal severe adult respiratory distress (6), third trimester hemorrhage (3), severe preeclampsia (1), bicatrical uterus (2), primiparous site (1)
Maternal outcome ICU Deaths Cause of deaths	13 patients, 9 intubated (ECMO (3)) 7 patients (from the patients intubated) Hemorrhage Shock (1), Septic Shock (1), Cerebral death (1), Respiratory Arrest (4)

Abbreviations: ECMO: Extracorporeal membrane oxygenation; PPRM: Preterm premature rupture of the membranes; DIC: disseminated intravascular coagulation; ELCS: elective c-section; EMCS: emergency c-section; HTN: hypertension.

Table 2:- Probability of survival in covid 19 positive patients.

Number	yes	non	P value
Moderate and or severe respiratory distress	15	25	0.267
hospital stay >16 days	6	34	0.038
flu syndrome	19	21	0.039
lymphopenia	20	20	0.012
D-dimers>500	19	21	0.007
LDH >500	3	37	0.814
Albumin<25	8	32	0.076
CRP>50	23	17	0.912
Cytolysis >2x la normal	5	35	0.096
Reanimation	13	27	0.724
ECMO	3	37	0.007
Intubation	9	31	0.085

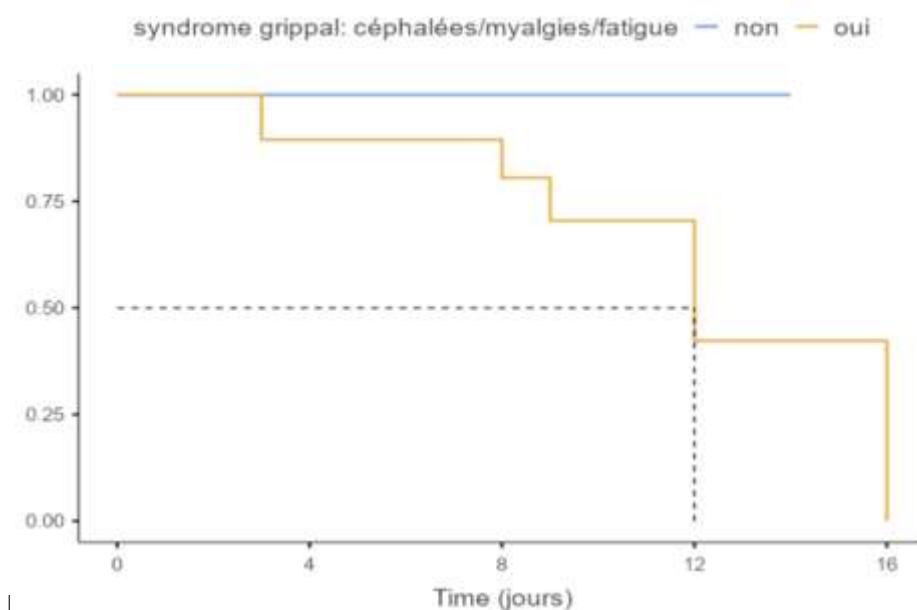


Figure 1:-Probability of survival based on flu syndrome in covid 19 positive patients.

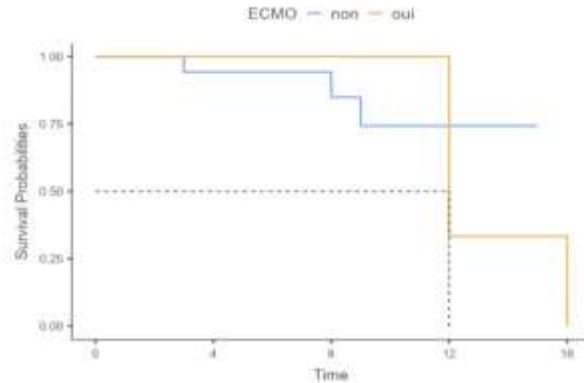


Figure 2:- Probability of survival based on ECMO in covid 19 positive patients.

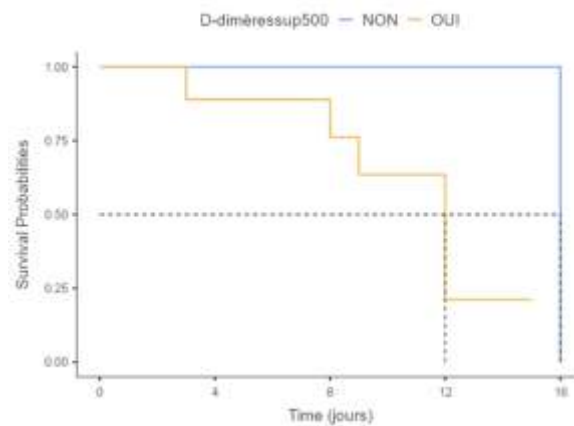


Figure 3:- Probability of survival based on D-dimer level in covid 19 positive patients.

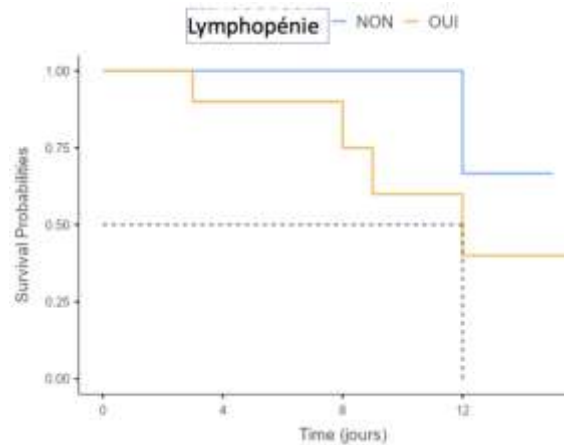


Figure 4:- Probability of survival based on lymphocyte count in covid 19 positive patients.

Discussion:-

According to John Allotey and al in the meta-analysis published on August 2020, including 77 studies and 11432 women, the overall rate of covid-19 infection in pregnant women and recently pregnant women attending or admitted to hospital was 10 % [9]. With lower immune functions, pregnant women represent a group at higher risk of developing the COVID-19 leading to more adverse outcomes [10,11]. There is no specific symptomatology to pregnant women and clinical signs remain comparable to those observed in the general population. According to the meta-analysis published by John Allotey and al, the most common symptoms reported by pregnant women with COVID 19 were fever (40%) and cough (39%) [9]. SARS-CoV-2 infection is thus manifested primarily by

respiratory symptoms, but a richer semiology is beginning to be reported with neurological, cardiac, renal, ophthalmic and dermatological symptomatology [12]. In the study conducted by Mao et al., 36.4% of the 214 patients included presented neurological signs. These signs were more common in the 88 patients with severe disease, who included confusion (14.8%), neuromuscular damage (19.3%) and stroke (5, 7%) [13]. In addition, cases of epilepsy and necrotic encephalopathy have been reported [14-16]. Finally, the viral neurological tropism could participate in the respiratory distress caused by SARS-CoV-2 [17]. As was the case in one of our patients admitted in the ICU, who presented an encephalopathy leading to a neurological deterioration, which could be linked to SARS-CoV-2. The RT-PCR study remains the gold standard for positive diagnosis. It can be carried out on different samples; RT-PCR on a nasal swab appears to be less sensitive (63%) but remains the most widely practiced [12]. It was indeed performed in all our patients via the nasopharyngeal route and was positive in 100% of cases. The chest x-ray and the thoracic computed tomography (CT) are added to the diagnostic arsenal [18]. Radiological aspects are the same as the rest of the population, ranging from predominantly inferior and subpleural unsystematized ground glass areas to bilateral alveolar condensations, at a more advanced stage [19]. However, in the case of pregnant women, the real concerns remain the teratogenic effects of ionizing radiation on the fetus. It is reassuring that the fetal radiation dose for routine chest CT is 0.03 mGy and that exposure to radiation doses inferior to 50 mGy is not associated with an increased risk of fetal abnormalities or miscarriage [20]. However, in our series, only women in their third trimester with mild to severe respiratory symptoms received a chest CT scan (16 patients), which showed typical patchy solid consolidation consistent with COVID19 pneumonia in all patients. Patients with lung disease in general, are at greater risk of premature rupture of membranes, preterm deliveries, fetal death in utero, intrauterine growth restriction and neonatal death. According to the meta-analysis conducted by Allotey and al, the overall rate of preterm birth was 17% and that of spontaneous preterm birth was 6%. Compared to women without the disease, the odds of preterm birth were higher, but no difference was observed for other maternal complications which complements our findings, with a higher preterm birth rate (24%) [9]. Furthermore, the rate of C-sections in our cohort was 23/36 (63,8%), which is higher than the rate of C-sections in Morocco (21,2%,) [21]. Compared to non-pregnant women of childbearing age with COVID-19, the odds of ICU admission and the need for invasive ventilation were higher in pregnant women and recently pregnant women [9]. Nine of the severe cases progressed to requiring intubation and ventilation, three of them were in the second trimester, and six in the third trimester. With 13/40 (32,5%) women admitted to the ICU, and 17,5% mortality rate we amounted to the same conclusions, as those of numerous studies documented in scientific literature where the mortality rate of pregnant patients is as high as 25 % compared to 10 % in the general infected population [22,23].

Strengths and Limitations

We are acknowledging that our study is limited by the small sample size, our findings are important for understanding the characteristics of the disease in pregnant patients.

Conclusion:-

Although our cohort of 40 patients with confirmed COVID-19 was relatively small in absolute numbers, we have prospectively collected data for the ten months' period covered. There is a relatively higher rate of preterm birth, and C-section for patients with COVID-19 however development of severe neonatal COVID-19 complications seemed reassuringly rare. Our findings can provide an additional guidance to enhance prenatal counselling of patients with COVID-19 infection during pregnancy.

Declaration of Competing Interest

The authors report no declarations of interest.

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