The National Early Warning Score adapted to pregnancy in case of suspicion of COVID-19 infection: evaluation in a retrospective study.

Louise Ghesquiere[1], marc lambert[2], cecile yelnik[2], Mercé Jourdain[3], Fanny Vuotto[3], Damien Subtil[4], Karine Faure[3], and Charles Garabedian[4]

[1]CHRU Lille, hopital Jeanne-De-Flandre
[2]Affiliation not available
[3]CHRU de Lille
[4]Jeanne De Flandre

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Abstract

Objective - Determine what is the best initial clinical score to evaluate and propose adequate management to pregnant women with suspicion of COVID-19 infection. Design – setting – population: Retrospective study in one center (Lille, France) from 15 March 2020 to 15 April 2020. Were included all pregnant consulting in our emergency center for a suspicion of COVID-19 infection. Methods – main outcome measures: Women had a clinical, radiologic and biologic first evaluation to adapt management at home or in hospitalization. The National Early Warning Score (NEWS) and the NEWS-PREG, which is an adaptation including trimester of pregnancy, were calculated in posteriori for each patient. Sensitivity, specificity, predictive positive and negative value of these scores to propose adequate management were calculated. Results: 63 women were included. Seventeen were hospitalized (27%) among 4 in intensive care (6,5%). Sensitivity, specificity, predictive positive value and predictive negative value to predict hospitalization of the NEWS were respectively 52.9%, 100%, 100% and 85.2%. There were respectively 82.4%, 93.5%, 82.4% and 93.4% for the NEWS-PREG. Areas under the curve to predict hospitalization of the two scores were 0.77 for the NEWS and 0.88 for the NEWS-PREG. No woman was readmitted or had to be transferred from conventionel hospitalization to intensive care within 48 hours of her initial assessment and orientation. Conclusion: The NEWS-PREG is an interesting initial clinical score which can be used in case of suspicion of COVID-19 infection to propose adequate management. It will be interesting to evaluate in a prospective study.

Main text:

Introduction

The current pneumonia outbreak of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been declared a pandemic by the World Health Organization (WHO) on March 11, 2020[1.] Pregnant women and their fetuses represent a high-risk population during infectious disease outbreaks[2-5]. In 215 pregnant women admitted for delivery in New York, 33 patients were SARS-CoV-2 positive (15,4%) with 4 symptomatic (1,9%) and 29 asymptomatic (13,5%)[6]. Pregnancy complications included delivery by cesarean section (84%), preterm labor < 37 weeks (24.3%), premature rupture of membranes (20.7%), preeclampsia (16.2%), fetal growth restriction (11.7%). Di Mascio et al. described a rate of perinatal death at 7-11% and 57.2% of new born were admitted to the neonatal intensive care unit. Vertical transmission is unlikely and still discussed[7]. Serious morbidities were reported in 3% of pregnant women with COVID-19 as they required ICU care with mechanical ventilation[8].

Different guidelines have been published by international expert consensus or national society or experts[2,9-12]. However, none proposed a score for the initial clinical examination which could help the clinician in their algorithm of decision. The National Early Warning Score (NEWS) determines the degree of illness of a patient using six physiological findings and one observation[13]. It has been tested in many situations and has the ability to discriminate patients at risk of morbidity or mortality[13-15]. This score or its second version is also used in studies evaluating treatment in severe COVID-19 situations[16]. In the context of the actual pandemic, Liao et al. proposed a modified version of the NEWS with age [?] 65 years added for early recognition of patients with severe COVID-19 infection and admission decisions according to the severity classification[17].

In the same way, we proposed a modified one including the trimester of pregnancy, the NEWS-PREG, with the objective to help the decision of the clinician during the initial evaluation of a pregnant woman with a suspicion of COVID-19 infection. Therefore, the objective of our study was to determine if the NEWS and the NEWS-PREG were able to evaluate and propose adequate management to pregnant patients with suspicion of COVID-19 infection.

Methods

This retrospective cohort study was conducted in one center (Lille, France) from 15 March 2020 to 15 April 2020. Were included all pregnant consulting in our emergency center for a suspicion of COVID-19 infection. During this consultation, women had a clinical examination and then radiologic (chest X-ray or CT scan) and laboratory test. The clinical evaluation included an interrogation on comorbidities and COVID-19 symptoms (cough, fever, dyspnea, rhinitis, chest tightness, headache, myalgia, anosmia-agueusia, gastrointestinal symptoms) as well as their date of appearance. The radiologic evaluation researched sign of COVID-19 described in literature (pneumonia, ground glass opacities, consolidations, multifocal lesions...)[18]. Laboratory test results were compiled, including standard blood counts (absolute white blood cells, neutrophils and lymphocytes) and C-reactive protein[19]. All women had a quantitative Reverse transcriptase-polymerase chain reaction (qRT-PCR) to confirm COVID-19 infection via nasopharyngeal swab test. The qRT-PCR result was obtained 24h-48h after the swab test. Depend clinical symptoms, chest-X ray or pulmonary CT scan and routine blood test, women returned at home or were admitted to an isolated suite or intensive care in our hospital.

For each patient, we retrospectively calculated the NEWS and the NEWS-PREG (Table 1). The NEWS is a score based on 8 parameters: age (years), respiration rate (/mn), oxygen saturations, need for supplemental oxygen, systolic blood pressure (mmHg), heart rate (bpm), consciousness and temperature (°C). Each parameter is set between 0 and 3. In complement with the NEWS, due to the particular situation of the pregnancy, we proposed the NEWS-PREG (Table 1). We have replaced the age as proposed by Liao et al., by the trimester of pregnancy. The second trimester is set 1 point and the third trimester is set 2 points. We made this choice to adapt it in function of pregnancy trimester regarding the literature on pandemic 2009 Influenza A(H1N1) and influenza that found a higher risk of mortality in the second and third trimester[20,21]. Thus, particular attention should be given to pregnant women in the second and in the third trimester. After calculation of the score, inpatient management is proposed in case of a score greater than or equal to 5 [17]. The evolution of the patient 2 days after her first consultation was noted to determine if the patient was well classed during her first evaluation. The principal endpoint was to determine what was the best evaluation initial between NEWS and NEWS-PREG. The secondary objective was to compare characteristics (clinic, biologic and radiologic) of patients managed at home with patients hospitalized.

Statistical analysis

Categorical variables are described as numbers and percentage. Continuous variables are reported as median (1st quartile; 3rd quartile). A nonparametric Mann-Whitney U test was used for intergroup comparisons of continuous variables. Categorical variables were analyzed with a Khi2 test or Fisher test. A p value <0 .05 was considered significant. ROC analysis was performed to evaluate the ability of NEWS and NEWS-PREG to predict the patient hospitalization. An area under the ROC > 0.80 was considered significant.

We determined sensitivity, specificity, positive predictive value and negative predictive value of NEWS and NEWS-PREG to predict hospitalization. The tests were performed using the IBM SPSS statistics 20.0.

Results:

Sixty-three women were included. Table 2 reports the characteristics of the population. The median age of patients was 31 (26.8; 33.8) years. Gestational age at first consultation was 24 (18; 30.1) weeks of gestation with 14 patients in first trimester (22.2%), 27 in second trimester (42.9%) and 22 in third trimester (34.9%). In median, women consulted 6 days after first COVID-19 symptoms (3; 9 days). Principal symptom was cough (76.2%). The others symptoms were headache (39,7%), fever (34,9%), dyspnea (36.5%), rhinitis (33,3%), myalgia (27%), chest tightness (22,2%), anosmia-ageusia (20,6%). In these 63 women, 14 had a PCR COVID-19 positive (22.2%). 17 were hospitalized (27%) among 4 in intensive care (6,5%). Clinical symptoms more frequent at women confirmed COVID-19 positive were cough (85.7%), fever (50%), headache (57.1%), myalgia (42.9%) and dyspnea (35.7%). 35.7% were hospitalized (5/14).

The median of NEWS was 1 (0.5-3) and of the NEWS-PREG was 3 (1-5). For all the population, sensitivity, specificity, predictive positive value and predictive negative value to predict hospitalization of the NEWS were respectively 52.9%, 100%, 100% and 85.2%. There were respectively 82.4%, 93.5%, 82.4% and 93.4% for the NEWS-PREG. Areas under the curve of the two scores to predict hospitalization were 0.77 for the NEWS and 0.88 for the NEWS-PREG (Figure 1).

No woman was readmitted or had to be transferred from conventionel hospitalization to intensive care within 48 hours of her initial assessment and orientation.

In women with NEWS-PREG < 5, three were hospitalized. For these 3 women, radiologic and biologic exams were abnormal with interstitial syndrome and inflammatory syndrome. In the contrary, 3 women with NEWS-PREG = 5 were not hospitalized. For these patients, the chest X-ray was normal and the outcome was good. All women with NEWS-PREG > 6 (n=10) had chest X-ray abnormalities and 90% (9/10) had an inflammatory biologic syndrome.

Table 3 shows the comparison between patients managed at home and hospitalized. There were no significant difference in gestational age between the two group with a tendency of lower gestational age in women managed at home (22.6 WG (14.2-30) vs 27.5 WG (21.8-32.7), p=0.065). More comorbidity were observed in the hospitalization group with 35.3% of obesity, 23.5% of pulmonary disease and 17.6% of gestational diabetic. There was no significant difference between two groups concerning numbers of positive qRT-PCR to confirm COVID-19 infection. Concerning clinical symptoms, dyspnea was significantly more frequent in the hospitalization group (56.3% vs 28.3%, p<0.05). Headache and diarrhea were significantly more frequent in the no hospitalization group (respectively 47.8% vs 12.5% and 21.7% vs 0%). Clinical evaluation founded NEWS and NEWS-PREG significantly higher in hospitalization group, respectively 5 (3-6.5) and 6 (5-8), than in no hospitalization group, 1 (0-1.25) and 2 (1-3), p<0.001. In hospitalization group, there were more abnormal chest X-Ray or CT scan (82.4% vs 5.1%, p<0.05) and more inflammatory syndrome (76.5% vs 12.5%, p<0.05).

Discussion:

Main findings:

Due to its potential gravity, it is important in COVID-19 disease to early recognize and propose adequate management especially for pregnant women. A physiological parameter-based warning score adapted for pregnant women, the NEWS-PREG, was evaluated in our center to facilitate early recognition of patients with severe infection and admission decisions according to the severity classification. The sensibility, specificity, predictive positive and negative value were higher than 80% (respectively 82.4%, 93.5%, 82.4%, 93.4%) and none women were changed orientation during the 48h after her initial evaluation. This score seemed more adapted to pregnant women than the NEWS with a better sensibility and a better AUC. Thus, this score could help clinicians in the initial clinical evaluation of pregnant women with COVID 19 suspicion and could be a complement to previous algorithms and recommendations published [9,22,23]. Its association

with comorbidity and radiologic exam results in the initial evaluation would further improve management of pregnant women.

Characteristics of patients in our population were similar of previous studies[24-26]: principal symptoms were cough (76.2%), fever (34.9%), dyspnea (36.5%) and headache (39.7%). In COVID-19 positive patients confirmed (RT-PCR positive), there were more fever (50%), myalgia (42.9%) and headache (57.1%). In review of COVID-19, in pregnant women with COVID-19, the most common symptoms were fever (54%), cough (35%), myalgia (17%), dyspnea (12%) and diarrhea (4%). Clinical symptom that seemed to be more predictive of severity and hospitalization was dyspnea with a significant difference between two groups. Symptoms that seemed to be more predictive of no severe disease were diarrhea and headache.

Women hospitalized had initial NEWS and NEWS-PREG higher than women managed at home and had more severe disease. These confirm efficiency in clinical score for initial women evaluation and orientation. In addition to this clinical evaluation, recommendation proposed the search of a radiological evaluation [12,18,22,23]. Chest X-Ray or CT scan shown more abnormalities in hospitalization group (82.4% versus 5.1%). It was observed, as previously described, ground-glass opacities or mixed ground-glass opacities, consolidations, peripheral distribution, bilateral involvement, be lower lung predominant and multifocal[18,22,27]. These typical lesions can be helpful in early screening of highly suspected cases and in evaluation of the severity and extent of the disease. Indeed, Chest CT scanning has high sensitivity for diagnosis of COVID-19 and in a pregnant woman with suspected COVID-19 infection, a chest CT scan may be considered as a primary tool for the detection of COVID-19 in epidemic areas[23].

Strengths and limitations:

None score has actually been proposed for initial clinical evaluation of pregnant women with suspicion of COVID-19 infection. This score is adapted from the National Early Warning Score (NEWS), a score known to discriminate the initial severity of patients used early warning scoring systems based on the derangement of patients' vital signs variables (e.g., pulse rate, breathing rate, blood pressure)[13,15,28,29]. The sum of the allocated points is used to direct care involve more experienced staff or call a rapid response team. Its second version is also used in studies evaluating treatments for COVID 19 infection[16]. We made the choice to adapt it in function of pregnancy trimester regarding the literature on pandemic 2009 Influenza A (H1N1) and influenza. Indeed, Siston et al. reported the outcome of 788 pregnant women in the United States with 2009 influenza A (H1N1) [20]. Among those, 30 died, 4 during the first trimester (7.1%), 15 in the second (26.8%) and 36 in the third (64.3%). This higher risk of mortality is also observed in the influenza[21]. Thus, particular attention should be given to pregnant women in the second and in the third trimester.

Tested in our population, this score shown encouraging results with high specificity and predictive negative value. However, six patients were managed differently as we proposed with the NEWS-PREG. Three patients had a NEWS-PREG less than 5 but were hospitalized. For these 3 cases, the chest X-ray as well as the blood test were abnormal explaining their hospitalization. It is known that in some forms of COVID-19, the clinic evaluation can be reassuring, but that the chest X-ray or CT scan can be worrying and requires inpatient monitoring for the risk of rapid clinical worsening [27,30]. Three cases had a NEWS-PREG [?] 5 and were not hospitalized. For these three cases, chest X-ray and blood test were reassuring with no abnormality and evolution was good with home management.

Our study has limitations. The sample size was small in the NEWS-PREG [?]5 group. Majority of pregnant women who consulted for a suspicion of COVID- 19 were in mild or asymptomatic degree. Only 14 women had a RT-PCR positive probably due to the lack of sensibility of RT-PCR.

Conclusion

NEWS-PREG could be used to evaluate and propose management of pregnant women with suspicion of COVID-19. It could help the clinician for initial evaluation as also radiological and biological examination. Moreover, this score is based on physiological parameters easy to obtain in emergency centers and its interpretation is also simple. It will be interesting to evaluate it prospectively and in a larger cohort.

Disclosure of Interests:

All authors report no conflict of interest.

Contribution to Authorship:

All of the authors participated. L. Ghesquiere, M. Lambert, C. Yelnik, M. Jourdain, F. Vuotto, D. Subtil, K. Faure, C. Garabedian supervised and corrected this article. C. Garabedian is the principal investigator of the study. L. Ghesquiere, M. Lambert, F. Vuotto participated to include patients. L. Ghesquiere did the statistic analysis. L. Ghesquiere written article. C. Garabedian, C. Yelnik, M. Lambert reread the article.

Details of Ethics Approval:

The study was approved by the local committee of the national ethical commission (CNIL NdegDEC20-114 on 04/17/2020).

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Table 1: NEWS-PREG

PARAMETERS	2	1	0	1	2	3
Weeks of gestation				15-27	28-42	
Respiration rate (/mn)	? 8	9-11	12-20		21-24	? 25
Oxygen saturations	? 91	92-93	94-95	? 96		
Any supplemental oxygen		Yes	No			
Systolic BP (mmHg)	? 90	91-100	101-110	111-219		? 220
Heart rate (bpm)	? 40	41-50	51-90	91-110	111-130	? 131
Consciousness			Alert			Drowsiness Lethargy Coma Confusion
Temperature (°C)	? 35.0	35.1-36.0	36.1-38.0	38.1-39.0	? 39.1	

BP: Blood Pressure

Table 2 – Demographic and Clinical Characteristics of Pregnant Women

	All patients (N=63)	COVID+ (N=14)
General Characteristics		
Age (years)	31 (26.8; 33.8)	29.3 (25.9; 31.2)
Gestational age (WG)	24 (18; 30.1)	24.6 (18.3; 29.8)
Comorbidity BMI>30 Pulmonary disease Gestational Diabetic	7 4 4	3 1 3
Signs and symptoms		
Time (days) between the beginning of symptoms and first consultation	6 (3; 9)	8 (4; 9)

	All patients (N=63)	COVID+ (N=14)
Cough	48 (76.2%)	12 (85.7%)
Fever	22 (34.9%)	7 (50%)
Dyspnea	23 (36.5%)	5 (35.7%)
Rhinitis	21 (33.3%)	4 (28.6%)
Chest tightness	14 (22.2%)	2 (14.3%)
Headache	25 (39.7%)	8 (57.1%)
Myalgia	17 (27%)	6 (42.9%)
Anosmia-agueusia	13 (20.6%)	4 (28.6%)
Diarrhea	10 (15.9%)	2 (14.3%)
Inflammatory syndrome at the blood test	14 (22.2%)	5 (62.5%)
Abnormal Chest X-Ray or CT Scan	16 (25.4%)	7 (58.3%)
Hospitalization	17 (27%)	5 (35.7%)
Conventional	13 (20.6%)	4 (28.6%)
Intensive care	4 (6.3%)	1 (7.1%)

BMI = Body Mass Index; WG = weeks of gestation. Data are on median (1st quartile; 3rd quartile) or N (%)

Table 3 – Characteristics of the population according to hospitalization or no.

	No hospitalization (n=46)	Hospitalization (n=17)	p
General Characteristics			
Age (years)	31.3 (28.1; 34.1)	29.3 (24.7; 33.1)	0.253
Gestational age (WG)	22.6 (14.2; 30.0)	27.5 (21.8; 32.7)	0.065
Comorbidity BMI>30 Pulmonary disease Gestational Diabetes	1 (2.1%) 0 (0%) 1 (2.1%)	6 (35.3%) 4 (23.5%) 3 (17.6%)	0.001 0.004 0.057
RT-PCR COVID +	9 (19.6%)	5 (29.4%)	0.498
Signs and symptoms			
Time (days) between the beginning of symptoms and first consultation	7 (3; 10)	3.5 (1; 8.75)	0.042
Cough	33 (71.7%)	14/16 (87.6%)	0.314
Fever	15 (32.6%)	7/15 (46.7%)	0.325
Dyspnea	13 (28.3%)	9/16 (56.3%)	0.044
Rhinitis	18 (39.1%)	3/16 (18.8%)	0.138
Chest tightness	10 (21.7%)	4/13 (30.8%)	0.485
Headache	22 (47.8%)	2/16 (12.5%)	0.012
Myalgia	12 (26.1%)	4/16 (25%)	1.000
Anosmia-agueusia	12 (26.1%)	1/8 (12.5%)	0.663
Diarrhea	10 (21.7%)	0	0.052
Score NEWS	1 (0; 1.25)	5 (3; 6.5)	<0.0001
Score NEWS-PREG	2 (1; 3)	6 (5; 8)	<0.0001

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	No hospitalization (n=46)	Hospitalization (n=17)	p
Inflammatory syndrome Blood test Infl. Sd at the blood test	8 (17.4%) 1/8 (12.5%)	17 (100%) 13 (76.5%)	<0.0001 0.007
Abnormal Chest X-Ray or CT Scan	2/39 (5.1%)	14 (82.4%)	<0.0001

BMI = Body Mass Index; WG = weeks of gestation. Data are on median (1st quartile; 3rd quartile) or N (%). p<0.05 is significant.

Figure 1 : ROC curves of prediction of hospitalization

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AUC : Area under curve