

COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals

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Condensation: In a series of 43 COVID-19-positive pregnant women identified over a two-week period, infection was often asymptomatic, supporting a role for universal testing of pregnant women being admitted to the Labor Unit.

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Abstract:

The novel coronavirus 2019, or COVID-19, infection has rapidly spread through the New York metropolitan area since the first reported case in the state on March 1, 2020. New York currently represents an epicenter for COVID-19 infection in the United States, with 84,735 cases reported as of April 2, 2020. We previously presented an early experience with seven COVID-positive patients in pregnancy, including two women who were diagnosed with COVID-19 following an asymptomatic initial presentation. We now describe a series of 43 test-confirmed cases of COVID-19 presenting to a pair of affiliated New York City hospitals over two weeks from March 13 to 27, 2020. Fourteen (32.6%) patients presented without any COVID-associated viral symptoms, and were identified either after developing symptoms during admission or following the implementation of universal testing for all obstetrical admissions on March 22. Of these, 10/14 (71.4%) developed symptoms or signs of COVID-19 infection over the course of their delivery admission or early after postpartum discharge. Of the other 29 (67.4%) patients who presented with symptomatic COVID-19 infection, three women ultimately required antenatal admission for viral symptoms, and an additional patient represented six days postpartum after a successful labor induction with worsening respiratory status that required oxygen supplementation. There were no confirmed cases of COVID-19 detected in neonates upon initial testing on the first day of life. Applying COVID-19 disease severity characteristics as described by Wu et al, 37 (86%) women possessed mild disease, four (9.3%) exhibited severe disease, and two (4.7%) developed critical disease; these percentages are similar to those described for non-pregnant adults with COVID-19 infections (about 80% mild, 15% severe, and 5% critical disease).

Introduction:

In December 2019, a novel coronavirus was first reported in Wuhan, in the Hubei province of China.[1] Over the ensuing months, widespread transmission of SARS-CoV-2, the virus that causes COVID-19, has been reported in every inhabited continent. The United States now has the highest number of test-confirmed COVID-19 infection worldwide, with current estimates of 213,144 test-confirmed cases and 4,513 deaths as of this writing.[2] New York in particular has been designated a “hot spot,” due to a high proportion of test-confirmed cases, with 84,735 cases reported in New York State and substantial disease burden in New York City.

While data regarding COVID-19 continues to inform our understanding of this disease, information specific to pregnancy remains limited.[3] In prior pandemics such as SARS and H1N1, pregnant women were more susceptible to serious illness and had greater mortality rates than the general population.[4] Data regarding the clinical characteristics of SARS-CoV-2 infection in pregnant women remain to be determined. Here, we present our experience with test-confirmed COVID-19 cases in pregnancy presenting to an affiliated pair of New York City hospitals over two weeks between March 13 and March 27, 2020.

Methods:

Study design and patients

We performed a retrospective review of medical records over a 15-day period beginning with the first polymerase chain reaction (PCR)-confirmed COVID-19 infection involving a pregnant patient at our institution on March 13, 2020. Patients were diagnosed upon presentation to the Labor and Delivery Triage Unit, or during direct admission to the Labor Unit at either Columbia University Irving Medical Center (New York, NY) or the Allen Hospital (New York, NY), which are affiliated hospitals within the New York-Presbyterian Hospital system. Columbia University Irving Medical Center is a tertiary care referral center with approximately 4,600 deliveries per year, and the Allen Hospital is a closely affiliated community hospital with approximately 2,300 deliveries per year.

Early during the New York City COVID-19 pandemic (March 13 to 21, 2020), both hospitals screened all patients presenting to the Labor Unit at ≥ 20 weeks gestational age for signs, symptoms, or risk factors concerning for COVID-19, and restricted testing of pregnant women using criteria from our institutions' Infection Prevention and Control department. These criteria were based on symptoms including fever ≥ 37.8 C (100.0 F), dry cough, dyspnea, myalgias, or headache, as well as known COVID-19 exposures and/or recent travel. Specific to the COVID-19 outbreak, fever was defined by IP&C as a temperature of at least 37.8 C (100.0 F). If the patient required admission and had no alternative explanation for these symptoms, COVID-19 testing via a SARS-CoV-2 quantitative PCR nasopharyngeal swab was sent in addition to a respiratory pathogen panel PCR. If the patient did not require admission, but had COVID-19 symptomatology, testing was sent after review and approval by the Infection Prevention and Control department. Women were discharged home for outpatient follow up if they had stable vital signs, did not have an oxygen requirement, denied significant shortness of breath or respiratory symptoms, and were deemed suitable for telehealth follow up. After multiple healthcare workers were exposed with inadequate personal protective equipment using this initial approach [5], as of March 22 we initiated universal COVID-19 testing for all patients admitted to the Labor Unit in addition to symptomatic triage presentations, regardless of whether they possessed viral symptoms or other at-risk history.

This study was reviewed and approved by the Institutional Review Board under a waiver of informed consent.

Data collection

We reviewed clinical documentation for all pregnant women who tested positive for COVID-19 via SARS-CoV-2 PCR obtained by nasopharyngeal swab. Records related to neonates born to COVID-19 positive women were also reviewed.

Statistical analysis

Demographic variables that were continuous and normally distributed were expressed as means with standard deviations. Nonparametric continuous variables were expressed as medians with interquartile ranges. All data were tested for normality with the appropriate

result, median versus mean presented. Categorical variables were expressed as number and percent. In reporting outcomes, women are divided into two groups: (i) those who presented symptomatically and (ii) those who were asymptomatic and detected by screening.

Results:

A total of 43 pregnant women tested positive for COVID-19 infection from March 13 to March 27. This included seven women identified prior to universal SARS-CoV-2 PCR testing and 36 diagnosed during the period of universal SARS-CoV-2 PCR testing.

Patient characteristics

Demographics of our cohort are listed in Table 1. Maternal age ranged from 20 to 39 years with a mean age of 26.9 ± 5.9 years. Median gestational age at presentation was 37 0/7 weeks (Interquartile Range [IQR] 32 4/7, 38 6/7). The majority of women were obese, with a BMI ≥ 30 (n=26, 60.5%). The mean BMI for the cohort was 30.9 ± 5.3 kg/m² and two women (4.7%) had a BMI of 40 or greater. Eighteen women (41.8%) had an additional comorbid condition, with mild-intermittent asthma (n=8, 18.6%) representing the most common co-morbidity. Other comorbid conditions included type 2 diabetes mellitus (n=3, 7.0%) and chronic hypertension (n=3, 7.0%). Patients mostly resided in the Bronx (n=21, 48.8%) or upper Manhattan (n=19, 44.2%), and one was from out of state.

Of the 43 women in this cohort, three (7.0%) were initially admitted for COVID-19 symptoms, 18 (41.9%) were admitted for obstetric reasons, and the remaining 22 (51.2%) were deemed stable and received exclusively outpatient management. One previously symptomatic patient was notably readmitted on postpartum day six due to worsening respiratory symptoms. Obstetric reasons for primary admission included preterm labor (n=1) scheduled term cesarean (n=1), term labor (n=7), and term labor induction (n=9). Among term labor inductions, five were obstetrically indicated (reasons included cholestasis of pregnancy, pre-gestational diabetes mellitus, worsening chronic hypertension, gestational hypertension, and decreased fetal movement) and four were elective at ≥ 39 weeks gestational age.

Applying COVID-19 disease severity characteristics as described by Wu et al, 37 (86%) women possessed mild disease, four (9.3%) exhibited severe disease, and two (4.7%) developed critical disease presentations (Figure).[6]

Patients with symptoms on presentation

Over the two-week study period, 29 of the 43 women (67.4%) presented for inpatient triage assessment, reported symptoms potentially consistent with COVID-19, and tested positive upon viral PCR study. Of these, 20 (69%) reported COVID-19 symptoms as a chief complaint and nine (31%) presented with primary obstetrical complaints but then were identified to be symptomatic upon routine screening. The most common symptom at presentation was a dry cough (n=19, 65.6%) followed by fever (n=14, 48.3%) and myalgias (n=11, 37.9%). Less commonly reported symptoms included headache (n=8, 27.6%), shortness of breath (n=7, 24.1%) and chest pain (n=5, 17.2%). Twenty-six

(89.7%) out of the 29 women had some combination of these symptoms. Ten (34.5%) women reported sick contacts.

Of the 29 symptomatic COVID-19 positive women, 25 (86.2%) were stable for discharge home, with normal vital signs, no need for supplemental oxygen, and no clinical indication for imaging or treatment. Vital sign parameters and symptom-related return precautions were reviewed prior to discharge home. These 25 women were followed for 14 days via telehealth with daily telephone calls for monitoring of symptoms and maternal well-being. None of these 25 women required admission for management of COVID-19 at initial presentation. However, four (13.8%) symptomatic patients required admission for obstetric indications, including 34-week preterm labor, term labor, term prelabor rupture of membranes, and 40 5/7-week labor induction.

Four (13.8%) of the 29 symptomatic COVID-19 patients who were initially cared for in the outpatient setting later re-presented with symptoms of worsening fevers or increased work of breathing that required admission. This occurred within a week of COVID-19 diagnosis for all four women. Three of these women were admitted to the obstetrical inpatient antepartum service, while a fourth woman was admitted to the medicine service six days postpartum. None of the antepartum women required oxygen supplementation upon admission. In consultation with infectious disease specialists, the first pregnant patient received hydroxychloroquine (600 mg orally every 12 hours for 1 day, followed by 400 mg daily for four days) along with ceftriaxone (1 g intravenous every 24 hours for two days) as treatment for possible super-imposed bacterial pneumonia. This patient had continued fevers prior to admission, with an admission temperature of 38.4 C. The second pregnant patient received supportive therapy with intravenous hydration only. This patient had a co-infection with parainfluenza virus and appeared unwell on presentation, but rapidly improved with intravenous hydration. The third pregnant patient received ceftriaxone (1 g intravenous every 24 hours for two days), azithromycin (500 mg orally daily for three days), and intravenous hydration. Despite these women having similar objective findings, they received different treatments after consultation with the infectious disease specialists, likely due to nuances in their clinical characteristics and evolving recommendations. The fourth patient required readmission six days postpartum, and seven days after COVID-19 test confirmation. This woman represented to care due to worsening COVID-19 symptoms and a new oxygen requirement. On presentation, her oxygen saturation was 92% on room air but was noted to drop to the high 80s% with movement. Additionally, she was tachypneic with a respiratory rate of 30-32 breaths per minute. She was placed on a non-rebreather facemask initially and eventually weaned to oxygen support via nasal cannula. Chest X-ray confirmed a bilateral multifocal pneumonia. She was admitted to the medicine step down unit following assessment by an ICU triage team. She was treated with oral hydroxychloroquine, with dosing as described above. She currently remains an inpatient.

Patients asymptomatic on presentation

In our overall cohort of COVID-19 test-positive pregnant women, 14 (32.6%) of 43 patients initially presented without COVID-19 associated symptoms. Two of these women initially presented for obstetrically indicated labor induction. Both developed symptoms

that mimicked obstetrical complications, yet were ultimately diagnosed with COVID-19 infection as part of a broad differential, as previously described by this group.[5] Both patients required postpartum admission to the ICU due to complications including respiratory distress. One of the two patients who required ICU readmission developed renal insufficiency and remains an inpatient receiving supportive care without current need for mechanical ventilation or dialysis. The other patient improved and was discharged home. Both of the babies have tested negative for COVID-19 infection.

The remaining 12 of 14 patients were asymptomatic on presentation, and identified as a result of universal testing upon Labor Unit admission for obstetric indications. Four (33%) of these 12 patients remained afebrile and asymptomatic throughout their delivery hospitalization and postpartum courses to date. Eight (66.7%) patients developed a fever ranging from 37.9 - 39.2 C (100.2 - 102.6 F) during their admission, five developed fever intrapartum and three postpartum. The five patients who developed intrapartum fever received antibiotics (ampicillin and gentamicin) for suspected intra-amniotic infection. Three of the patients with intrapartum fevers received misoprostol as part of their labor induction. Two of these women remained on antibiotics post-operatively for treatment of presumed endometritis. Of the three women who developed postpartum fever, none had focal findings on examination or clear etiologies for their temperature elevations. Of the eight women who were febrile after the asymptomatic diagnosis of COVID-19, none developed respiratory symptoms throughout delivery hospitalization. No patients had prolonged hospitalizations, with all women discharged home on either postpartum day two or three. All 13 discharged women are being followed per our outpatient COVID protocol by either daily telehealth or telephone visits. Of those who have been discharged home, 6 (46.2%) of the 13 have developed symptoms including cough, myalgias, chest pain, anosmia, and/or dysgeusia within the first seven days after positive swab result. None of these women have required a postpartum visit to the office or emergency room. The other seven remain asymptomatic to date (April 2, 2020).

Perinatal outcomes

Delivery characteristics

The 18 women who delivered included four symptomatic women upon initial presentation and 14 initially asymptomatic women, as described above. Eight women (44.4%) were delivered via cesarean section. Cesarean deliveries were performed for non-reassuring fetal heart tones (n=3), repeat cesarean (n=2), arrest of descent (n=1), arrest of dilation (n=1) and failed labor induction (n=1). Ten women (55.5%) had uncomplicated normal vaginal deliveries.

Anesthesia considerations

All 18 women received neuraxial anesthesia (either using intrapartum epidural analgesia, spinal, or combined spinal-epidural anesthesia). None had contraindications (such as thrombocytopenia or sepsis) to neuraxial procedure, no hemodynamic instability was noted in any of the cases, and no neurological complications were noted. One patient required intraoperative conversion to general anesthesia due to intraoperative hemorrhage, as previously described.[5]

Neonatal outcomes

All 18 infants had Apgar scores ≥ 7 at 1 minute and ≥ 9 at 5 minutes, and all were tested for COVID-19 infection via SARS-Cov2-19 PCR nasopharyngeal swab. Fifteen infants tested negative on day of life (DOL) 0, and two infants had unclear results on DOL 0 that were repeated and negative on DOL 1-2. The remaining infant had an 'indeterminant' test result, which was clinically managed as a 'presumptive negative' diagnosis, as this result may reflect low level detection. This infant was discharged home on DOL4 and is currently being followed in the COVID Nursery Clinic. The infant has no signs of COVID-19 infection on most recent follow up on DOL 6. Three of the 28 infants were admitted to the NICU: one for prematurity at 34 6/7 weeks, one for evaluation of a congenitally diagnosed multicystic dysplastic kidney after delivery at 39 5/7 weeks, and one for respiratory distress with concern for sepsis at 37 weeks. This neonate has tested negative for COVID-19 infection. None of the neonates had IgG or IgM SARS-Cov2-19 testing. All 18 infants, including the three initially admitted to the NICU, have since been discharged home. Healthy newborns either roomed in with their mothers in isolettes whenever possible or were cared for in an isolated nursery for babies of COVID-positive mothers throughout their stay. Mothers were asked to perform hand hygiene and wear a surgical mask at all times. Mothers rooming with babies were instructed to keep a 6-foot distance from their babies when possible. However, breastfeeding was encouraged with use of hand hygiene and maternal masking.

DISCUSSION:

Principle Findings

We found that COVID-19 infection in pregnant women presenting with obstetric complaints or for delivery is often asymptomatic, suggesting a role for universal testing of pregnant women being admitted to the Labor Unit. We further found that while many of these women ultimately developed symptoms, disease severity in this small cohort of pregnant patients - 86% mild, 9.3% severe, 4.7% critical - appeared similar to what is described in the literature for non-pregnant people.[7]

Results in the context of what is known

Our findings are similar to published case series from China of pregnant women with COVID-19 infection that show an overall favorable prognosis. However, these case series are small [8,12]. Chen et al [12] described nine cases of pregnant women affected by COVID-19 infection during pregnancy. None of these patients required ICU admission or mechanical ventilation. Liu et al described 15 cases of pregnant patients who developed COVID-19 infection. None of these women had pre-existing comorbidities and none required ICU-level care or intubation. Two of these women were asymptomatic at presentation and underwent testing due to epidemiological contact history. However, on CT evaluation lesions consistent with COVID-19 pneumonia were detected.[8] In contrast to these series, four patients in this experience had severe disease and another two women developed critical presentations that required ICU care. While overall numbers are small, based on this limited experience the course of COVID-19 when presenting in pregnancy appears roughly comparable to what is described outside of pregnancy. However, there are reasons why conclusions like this may be false and misleading. Non-

pregnant patients presenting to care during the COVID-19 outbreak generally present for worsening respiratory symptoms, whereas many pregnant women in this experience presented to care for ongoing obstetric reasons, and prior to the onset of upper viral symptoms or fever. Our policy of universal testing for women admitted for delivery both revealed an unexpected number of asymptomatic positives and also suggested a milder course, in general, for these pregnant women. A universal testing strategy may therefore be identifying a milder subset of asymptomatic or pre-symptomatic women who are currently under-represented in general population testing data, which is plagued by testing shortages and test rationing. As a result, there is a likely over-representation of sicker COVID-19 patients in these broad test-positive cohorts. On the other hand, the only ICU admissions in this series were of asymptomatic women, and so our findings must be interpreted with caution until more data become available.

There is evidence that during pandemics, there is a trend towards increased severity of disease among pregnant women.[4,9] During the 1918 influenza pandemic, among the 1,350 reported cases of influenza among pregnant women, the proportion of deaths was reported to be 27%.[4] Similarly, regarding the SARS virus, Wong and colleagues reported that approximately 50% of pregnant women who developed SARS required admission to the ICU due to low oxygen saturation, with approximately 66% of pregnant women admitted to the ICU requiring mechanical ventilation. The mortality rate was as high as 50% for these women who required ICU admission.[10] In the H1N1 2009 influenza virus outbreak, pregnant women were more than four times more likely to be hospitalized and were at increased risk of complications when compared to the general population.[11] Pregnant women may be more susceptible to respiratory pathogens and pneumonia in pregnancy compared with non-pregnant women due to the physiological adaptations of pregnancy, such as edema of respiratory tract mucosa, diaphragmatic elevation, and increased oxygen consumption, as well as pregnancy-related immuno-alterations.[8] These adaptive changes also make women less tolerant of hypoxia.[8] Therefore, until more evidence is available, there is reason to remain concerned for the clinical course of COVID-19 pregnant women, despite encouraging early experiences here and elsewhere.

Clinical implications

The novel coronavirus represents a major public health threat, and based on current trajectories for exponential disease growth it is reasonable to expect that a large number of potentially asymptomatic pregnant women will present for care. Our findings suggest that COVID-19 infection is frequently asymptomatic and should be considered in all pregnant women in areas of high disease prevalence.

Universal testing of all pregnant women upon admission for delivery has potential value for many reasons. First, it allows us to identify asymptomatic patients with COVID-19 infection, facilitating the early initiation of infection control precautions including isolation, since it is known asymptomatic people can shed virus.[13] Second, it allows us to preserve our already-limited PPE supplies among women proven to be test-negative. While testing turnover is currently suboptimal (at our hospitals it is on average 8 hours at the time of this writing), labor often extends beyond this time frame. Third, it provides

useful information for the well-baby and neonatal intensive care nurseries, as well as reassures mothers prior to interactions with their newborns. Although there is no current proof of vertical transmission or of transmission of the virus via maternal breast milk, viral shedding from asymptomatic or symptomatic women may also have implications in the management of neonates delivered to these women, with the possibility of neonatal infection from respiratory droplet spread or nosocomial infection [14]. Our findings of a large proportion of asymptomatic positive patients also supports more restrictive visitor policies, strict hand and respiratory hygiene precautions, and masking of all patients and birth partners, as well as the staff on the Labor Unit.

We also found that when common perinatal and postoperative infectious or respiratory complications (such as chorioamnionitis, fever, or postoperative shortness of breath) arise in untested women, COVID-19 infection should be part of the differential diagnosis and testing is indicated.

Research Implications

The implications of asymptomatic COVID-19 infection in pregnant women are just now being understood. This report may have important implications for obstetric practice during the pandemic, but our understanding will continue to evolve as we follow these and other similar patients. Ramifications for their infants and family members are also not clear, particularly if the patients never become symptomatic. Importantly, this manuscript does not provide the important denominator of total number of women tested for COVID-19 during the study period. This was an intentional decision given changing testing strategies over the study time period that we believe would limit conclusions. An evaluation of the COVID-19 detection rate with our current hospital testing strategy that includes universal testing of admitted patients is the focus of a planned follow-up study that is currently underway. Finally, we need more data to understand whether the virus is vertically transmitted. A case report showed elevated IgM levels in an infant 2 hours after cesarean birth, though the serial nasopharyngeal swabs to 16 days of life were all negative.[14] In our small series, no neonates have tested positive to date and are being followed serially.

Strengths and limitations

Due to high COVID-19 prevalence in New York City, we are able to provide the largest case series to date of pregnant women with COVID-19 infection, although admittedly this series remains small. This cohort also includes patients presenting for care at either of two affiliated hospitals with close proximity and similar clinical practices. There is also no loss to follow-up in this series. In areas with lower disease prevalence there may be a different rate of asymptomatic COVID-19 infected individuals, and our findings may not be generalizable to other centers or regions.

CONCLUSION:

COVID-19 disease severity in pregnant women - 86% mild, 9.3% severe, 4.7% critical – appears similar to that of non-pregnant adults. Our strategy of universal testing for

COVID-19 identified asymptomatic women with COVID-19 infection, many of whom subsequently developed temperature elevations or disease symptoms. We believe that a strategy including universal testing of all pregnant women admitted to the Labor Unit in addition to those who present for triage evaluation of symptomatic complaints has obvious benefits that should inform best practices to protect patients, their families, and the obstetrical providers who care for them. Further research is indicated to understand the true magnitude of risks and to improve management.

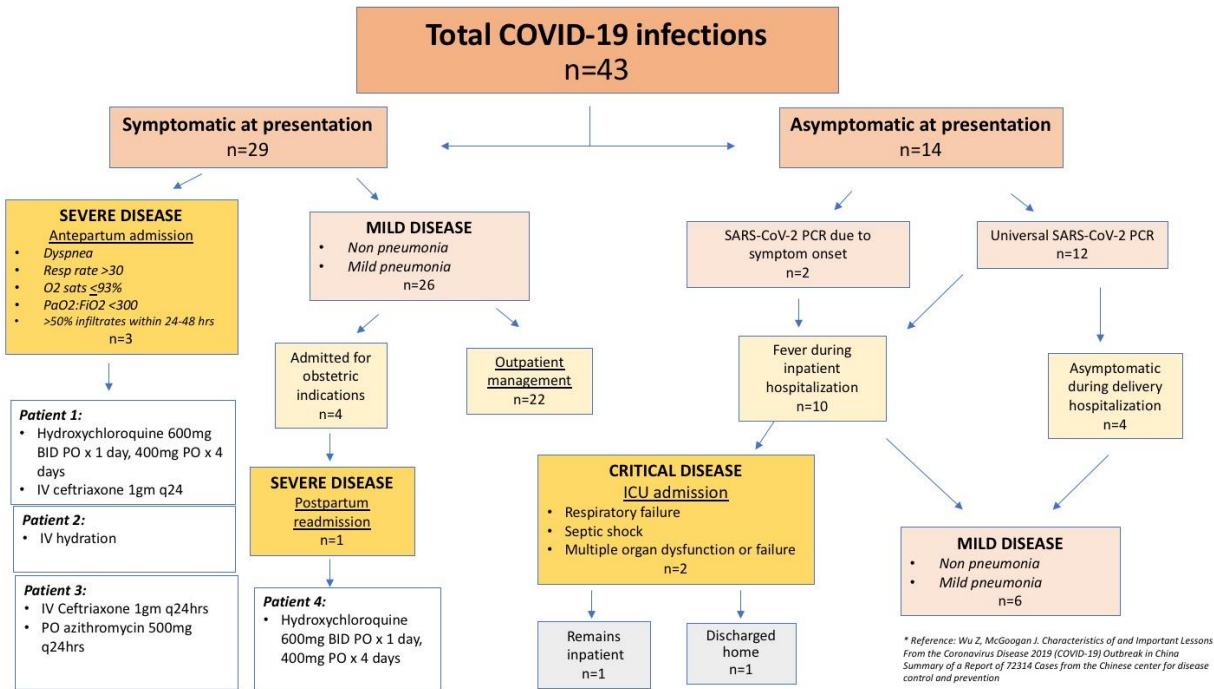
TABLE:

Table. Patient Characteristics

| | | | |
|---|------------------|----------|---------------|
| Demographics: | | | |
| Maternal age in years, mean \pm SD | 29.7 \pm 6.0 | | |
| Gestational age at diagnosis in weeks, median (IQR) | 37.0 (32.6-38.9) | | |
| BMI (kg/m ²), mean \pm SD | 30.9 \pm 5.3 | | |
| Co-morbid conditions*, % (95% CI) | 44.2 (30.4-58.9) | | |
| Signs and symptoms: | N= | % | 95% CI |
| Fever | 14 | 48.3 | 31.4-65.6 |
| Cough | 19 | 65.5 | 47.3-80.1 |
| Myalgias or fatigue | 11 | 37.9 | 22.7-56.0 |
| Dyspnea | 7 | 24.1 | 12.2-42.1 |
| Chest pain | 5 | 17.2 | 7.6-34.6 |
| Headache | 8 | 27.6 | 14.7-45.6 |
| Diarrhea | 0 | 0 | 0.0-11.7 |
| Sick contacts | 10 | 34.5 | 19.9-52.7 |
| Maximum temperature, mean (Celsius) \pm SD, range | 37.5 \pm 0.8 | | 36.4-39.4 |
| Disposition: | N= | % | 95% CI |
| Outpatient only | 22 | 51.2 | 36.8-65.4 |
| Admission (Antepartum) | 3 | 7 | 2.4-18.6 |
| Admission (Labor Unit) | 18 | 41.9 | 28.3-56.7 |
| Admission (Postpartum) | 1 | 2.33 | 0.1-12.3 |
| ICU admission | 2 | 4.7 | 1.3-15.5 |

* Comorbid conditions include: asthma, type 2 diabetes mellitus, chronic hypertension, thyroid disorder, seizure disorder, dermatological disease

FIGURE:



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