Title: Does COVID-19 restrictions affect detection and management of ectopic pregnancies? : Retrospective comparative analysis

Authors: Melissa A Deniz[1] and Johnson Amu[2]

1. Guys and St Thomas NHS Trust, London
2. Blackpool and Fylde coast NHS Trust, Blackpool

Corresponding Author: Melissa A Deniz

Dept Of Obgyne, St Thomas Hospital, Guys and St Thomas NHS Trust, Westminster Bridge Rd, Bishop's, London, SE1 7EH

Mobile: +447365432728

Email: melissa_deniz@hotmail.com

Shortened running title: Does COVID-19 restrictions affect ectopic pregnancies

ABSTRACT:

Objective: To assess impact of COVID-19 on diagnosis and management of ectopic pregnancy.

Design: Retrospective comparative analysis of ectopic pregnancies (EP) between January and July in 2019 (pre-COVID) and 2020

Setting: Performed at Blackpool Victoria Hospital, a district general hospital in Lancashire. There were no changes in health care personnel and EP management guidelines during both periods, however service provision was modified in line with COVID-19 regulations.

Population: We identified 27 EP cases of 1780 total pregnancies presented to early pregnancy unit (EPU) in 2019 compared to 22 cases of 1782 pregnancies in 2020.

Methods: Data was collected from EPU computerised database, looking at maternal age, site, side, size and gestation at diagnosis, ruptured EP, different management options. A Chi square statistical analysis compared the variables.

Main outcome measures: Gestation at diagnosis and cases of ruptured EP. Secondary outcome measures were the different management options.

Results: The incidence of EP cases was similar in 2020 and 2019 (22/1782; 1.23% Vs 27/1780; 1.51%, P=0.512). We found more cases of ruptured EP in 2020 compared to 2019 nonetheless statistically insignificant (6/22; 27.3% Vs 5/27; 18.5%, P=0.467). However, a stark difference noted was the gestation of EP diagnosis, 77.3% presented late (>6wks amenorrhoea) in 2020 compared to 2019, proving to be statistically significant (17/22; 77.3% Vs 25/27; 92.6%, P<0.001). Other parameters like maternal age, site and size of EP, and different management options; were not statistically significant.

Conclusions: We urge women to seek help as there are infection prevention measures in place, to provide the services required in early pregnancy.

Topic: Does COVID-19 restrictions affect the detection and management of ectopic pregnancies?

Introduction:

Pregnant women around the world have faced increased uncertainty with COVID-19, knowledge about the virus' impact on pregnancy is vital for treatment and prevention, the Medical Research Council (MRC) UK has funded several studies to investigate the potential impacts of COVID-19 at all stages of pregnancy. [1, 2]

Ectopic pregnancy is a common cause of mortality and morbidity. If not fatal, it leaves detrimental effect on a woman's emotional wellbeing and future fertility plans. When diagnosed early, patients are offered different management options depending on their clinical circumstances, but this usually may involve less invasive surgical intervention and complications. The ongoing pandemic may have affected patients' attitude to health and access to services provided by various early pregnancy units across United Kingdom. Our aim was to assess the impact of COVID-19 on the diagnosis and management of ectopic pregnancy.

Methodology: A retrospective comparative analysis of patients diagnosed with ectopic pregnancy (EP) between January to July in 2019 (pre-COVID) and 2020 in a district general hospital with 3000 deliveries per year. There were no changes to the health care personnel and EP management guidelines during both periods, however service provision in the early pregnancy unit (EPU) was modified in 2020 in line with COVID-19 regulations. Data was collected from patient notes and computerised database. We looked at maternal age, site, side and size of EP, gestation when EP was diagnosed, ruptured EP cases, different management options. A Chi square statistical analysis was done to compare the variables.

Results: We compared the total number of EP in the first seven months of 2020 with that of 2019 as a proportion of the total pregnancies in both years. The incidence of EP cases was similar in 2020 and pre COVID period (22/1782; 1.23% Vs 27/1780; 1.51%, P=0.512) although the presentation to EPU was much reduced during the lockdown period (Figure 1). We found more cases of ruptured EP in 2020 compared to 2019 but this was statistically not significant (6/22; 27.3% Vs 5/27; 18.5%, P=0.467). There was however, a stark difference at the gestation EP was diagnosed, 77.3% presented late (>6wks amenorrhoea) in 2020 compared to 2019 where majority of cases presented earlier (<6wks amenorrhoea); this proved to be statistically significant (17/22; 77.3% Vs 25/27; 92.6%, P<0.001). Other primary parameters were maternal age, site and size of EP, and different management (Conservative/Medical/Surgical) options; all of which were not found to be statistically significant. Table 1 denotes the results of the study as discussed.

Discussion: On analysis of the data, we had 1.51% (27/1780) of EP cases in 2019 similar to 1.23% (22/1782) in 2020 with equitable number of pregnancies in both years. Though statistically insignificant, we found large number of EP cases in February compared to June in 2019 and the exact opposite graph for 2020. This probably appears to correlate with the

initial lockdown introduced in UK and fears instilled in the minds of women regarding this unknown virus thus delaying presentation to EPU (Figure1).

There was no difference in maternal age, site and size of EP or the number of viable EP cases pre COVID and during COVID period. We noted 27.3% ruptured EP in 2020 confirmed at surgery while only 18.5% cases in 2019. While ruptured cases of EP bear a whole deal of clinical significance; viz requiring more invasive interventions, hospitalization, blood transfusions and future sequelae on fertility; this difference was not proven to be statistically significant. However, the gestation at diagnosis of EP was after a 6wks period of amenorrhoea in 2020(77.5%) while in 2019 majority were diagnosed prior to 6wks(92.6%) which is quite significant both clinically and statistically. We are well aware of the natural course of EP and the earlier they are diagnosed the better prognostic outcomes they hold. The later presentation of women to EPU after the introduction of COVID restrictions and delay in seeking appropriate medical advice for early pregnancy symptoms, is a plausible explanation for these findings. Similar findings were obtained in the North of Italy. [3, 4]

There is a debate with regards to the different treatment modalities during the pandemic [5]; Methotrexate a folate antagonist requires follow-up arrangements and being a chemotherapy agent comes with a minimum recommended period of six months prior to the next conception, but subsequent tubal patency and pregnancy were the same as laparoscopy [6]; it does cause further immunosuppression and increase susceptibility to Covid. There is scarce but growing evidence to support laparoscopic surgery with all the protective equipment and techniques to minimise aerosol generation and prevent transmission. [7, 8] We found that although the use of Methotrexate was nearly 20% higher post Covid; this was not found to be significant. (5/22; 22.7% Vs 1/27; 3.7%, P=0.077) Hence, clinicians should weigh the risks and benefits in each case depending on the presentation and provisions at their trust, at the same time bearing in mind to risk stratify patients for Covid when swabbing emergent cases may be difficult. [5]

Conclusion: While there are many ongoing trials to answer the various questions posed by the ongoing pandemic caused by COVID 19 and immense global effort now diverted towards finding an effective vaccine to curb its spread, we should not lose sight of the collateral damage caused due to lockdown restrictions and disruption of services including healthcare provision. [9]

At the brink of a potential second wave, it's imperative for clinicians to keep abreast with new guidance and evidence to support practice[10] and more importantly, to understand that ectopic pregnancy is a life threatening condition and in order to avoid fatal consequences we urge women to seek timely medical help and attend hospital appointments with the personal protection as advised nationally, with the assurance that necessary infection prevention measures are in place at all NHS trusts so as to continue to provide the services required in early pregnancy.[11]

Disclosure of interests: The authors of this manuscript have no conflicts of interest to declare.

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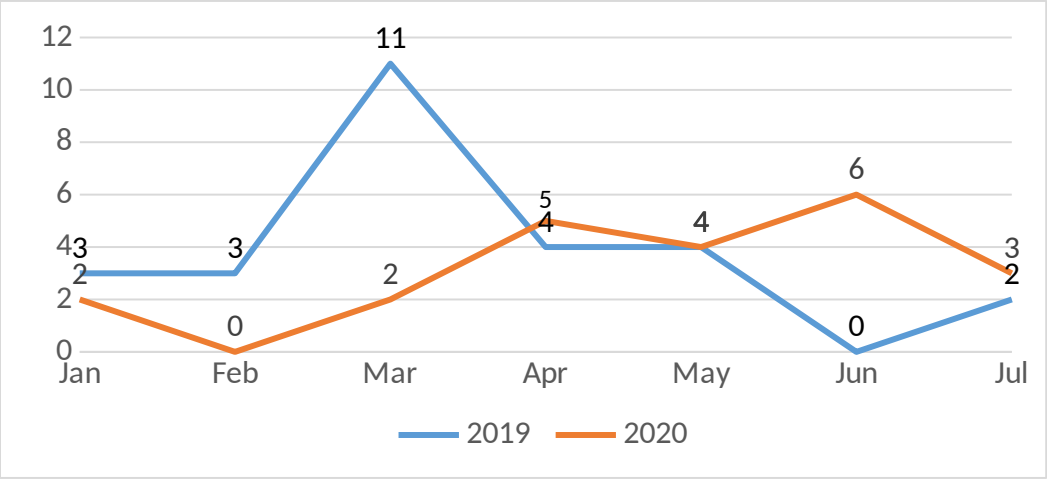
Figure 1:



Variable		2019	2020	*p* value
Number of ectopic cases/total pregnancies		27/1780 (1.51%)	22/1782 (1.23%)	0.512
Age in years n (%)	20-25 yrs.	9 (33.3)	5 (22.7)	0.818
	25-30 yrs.	7 (25.9)	6 (27.3)	
	30-35 yrs.	6 (22.2)	8 (36.4)	
	35-40 yrs.	3 (11.1)	2 (9.1)	
	>40 yrs.	2 (7.4)	1 (4.5)	
Side n (%)	Left	13 (48.1)	10 (45.5)	0.856
	Right	17 (62.9)	12 (54.5)	
Site of intact ectopic n (%)	Tubal	22 (81.5)	15 (68.2)	0.286
	Cornual	0	1 (4.5)	
Size of ectopic n (%)	<3cm	16 (59.3)	15 (68.1)	0.473
	3.1-6cm	5 (18.5)	5 (22.7)	
	>6cm	4 (14.8)	1 (4.5)	
GA at detection n (%)	<6wks	25 (92.6)	5 (22.7)	<0.001
	6-9wks	1 (3.7)	17 (77.3)	
	>9wks	1 (3.7)	0	

Ruptured n (%)	5 (18.5)	6 (27.3)	0.467
Viable n (%)	3 (11.1)	2 (9.1)	0.816
Laparoscopic management n (%)	22 (81.5)	14 (63.6)	0.159
Laparotomy n (%)	2 (7.4)	2 (9.1)	0.830
Methotrexate n (%)	1 (3.7)	5 (22.7)	0.077
Conservative n (%)	2 (3.7)	1 (4.5)	0.677

χ^2 = (1, N=3562) =0.512, p<0.01 (Table 1)