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Different Treatment Options for Tubal Ectopic Pregnancy: A Systematic Review

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ABSTRACT

Background: Treatment options for tubal ectopic pregnancy are: (1) surgery, such as salpingectomy or salpingostomy, either performed laparoscopically or by open surgery, (2) medical treatment, with a variety of drugs, that can be administered systemically and/or locally by various routes and (3) expectant management.

Objective: To be aware of the recent modalities in management of tubal pregnancy.

Methods: A systematic literature search of studies describing clinical trials published at the last twenty years was conducted. Literature searches of the PubMed and Cochrane Library databases were conducted. Using the following keywords: pregnancy, ectopic, tubal, interstitial, abdominal, angular, cornual, heterotopic, ovarian, gravidity, obstetric, cervical ripening, labor onset, labor presentation, trial of labor, treatment, therapeutics, therapy, medical, medication & surgical. The initial literature search identified articles were assessed for possible inclusion.

Results: Among the 62,588 women identified with ectopic pregnancy, 49,090 (78.4%) underwent surgery with salpingectomy or salpingostomy, while 13,498 (21.6%) received medical management with methotrexate. As can be seen in next figure, use of methotrexate increased significantly from 14.5% in 2011 to 27.3% by 2020 while surgical management declined from 85.5% to 72.7% over the same time period ($P < 0.001$).

Conclusion: Ectopic pregnancies account for the majority of first trimester maternal death. Tubal pregnancies account for the majority of ectopic pregnancies.

Keywords: Tubal ectopic pregnancy, Salpingostomy, Methotrexate.

INTRODUCTION

Ectopic pregnancy is an early pregnancy complication in which a fertilized ovum implant outside the uterine cavity. Implantation may occur anywhere along the reproductive tract with the most common implantation site being the fallopian tube. The incidence of ectopic pregnancy is 1% of pregnant women, and may seriously compromise women's health and future fertility. Currently, ectopic pregnancy can be often diagnosed before the woman's condition has deteriorated, which has altered the former clinical picture of a life-threatening disease into a more benign condition in frequently asymptomatic women [1, 2].

To improve the objective comparison of research outcomes in the diagnosis of ectopic pregnancy and to reduce clinical heterogeneity, a recent international consensus statement proposes uniformity in definitions of population, target disease and final outcome of women with a Pregnancy of unknown location (PUL) [3].

Adopting this consensus statement will hopefully lead to improved clinical care. A subgroup of ectopic pregnancies was identified being self-limiting and with spontaneous resolution without the need for an intervention. This new diagnostic category of women was defined as having trophoblast in regression (TIR) [4], a laparotomy to ligate the broad ligament and remove a ruptured tube. By 1885, **Tait** [5] had accumulated a relatively large number of successful cases of laparotomic salpingectomies. In 1985, **Chotiner** [6] was the first in English literature to describe a patient with tubal pregnancy treated successfully with systemic methotrexate. In 1999, the currently used term PUL was introduced for women with a positive pregnancy test and an inconclusive transvaginal ultrasound [7].

During the 1970s and 1980s laparotomy was gradually replaced by operative laparoscopic options. **Shapiro and Adler** [8] reported laparoscopic salpingectomy using electrocoagulation followed by excision for an ectopic pregnancy in 1973.

When methotrexate is administered systemically, it can either be given in a fixed multiple dose intramuscular regimen or in a variable dose intramuscular regimen. The fixed multiple dose regimen is derived from the treatment of gestational trophoblastic disease and is combined with folinic acid (citrovorum/ leucovorin rescue) to reduce chemotherapy toxicity [9, 10].

Only a few studies have been published describing expectant management in selected patients with small ectopic pregnancies without fetal cardiac activity, an upper limit for serum hCG concentration that continues to decline and/or a low serum progesterone concentration [11, 12].

Recent findings of no difference in fertility during the 2 years after an ectopic pregnancy when comparing medical treatment versus conservative surgery and conservative surgery versus radical surgery have answered some longstanding questions and raised new ones for determining the optimal management of ectopic pregnancies. These findings in particular have allowed consideration and weighing of a wider range of factors, including women's preferences, efficacy, and the period of monitoring until recovery [13].

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Pregnancy of unknown location can be a challenging clinical scenario, as false diagnosis can lead to major patient harm. Careful consideration of individual patient risk, test interpretation, and the harms of intervention versus expectant management must take place, and consultation with experienced providers should occur when a diagnosis is in doubt. The choice of medical, surgical or expectant management depends largely on the initial b-hCG level. Ultimate treatment choice should be individualized to a patient's circumstances and preferences [(14)].

Aim of the review was to be aware of the recent modalities in management of tubal pregnancy and to clarify the advantages and disadvantages of each modality and how suitable each of these treatment options for a certain patient.

Methodology:

A systematic literature search of studies describing clinical trials published at the last twenty years was conducted. Literature searches of the PubMed and Cochrane Library databases were conducted using the following keywords: pregnancy, ectopic, tubal, interstitial, abdominal, angular, cornual, heterotopic, ovarian, gravidity, obstetric, cervical ripening, labor onset, labor presentation, trial of labor, treatment, therapeutics, therapy, medical, medication & surgical. The initial literature search identified articles were assessed for possible inclusion.

Inclusion criteria:

Randomized controlled trials (RCTs) and observational studies, all types of treatments and medications for ectopic pregnancies, the long-term survival of patients with or without complications, successful pregnancy and birth.

Exclusion criteria:

Articles of failed treatments of ectopic pregnancies, articles with over all P value > 0.05, and articles for which the full text is not available in English.

Sample size: All articles fulfilling the inclusion criteria within the last twenty years.

The Perspective database (Premier, Charlotte and NC) was used to identify women 15–60 years of age with ectopic pregnancy treated from 2011 to the first quarter of 2020.

Demographic and clinical data included age at the time of the treatment (<20, 20–24, 25–29, 30–34, 35–39, 40–44, and ≥45 years), years of the treatment, marital status (married, single, and other/unknown), and primary insurance status (commercial, medicare, medicaid, uninsured, and unknown). Race was self-reported and categorized as white, black, Hispanic, and other/unknown. The Elixhauser comorbidity index, a measure of underlying medical comorbidity based on defined coding, was used to classify comorbid diseases in patients. The index was classified into 0, 1, and ≥2 based on the number of comorbid medical conditions.

Hospitals were categorized based on location (urban or rural), teaching status (teaching or non-teaching), hospital bed size (<400, 400–600, and >600 beds), and region of the country defined within the dataset (Northeast, Midwest, West, and South). Annualized hospital volume was calculated for each hospital and estimated as 4 times the quarterly mean of the number of patients with any treatment at a given hospital.

Outcomes:

The outcomes of the analysis included medical vs. surgical treatment, and salpingostomy vs. salpingectomy among women treated surgically. A composite metric of any complication was analyzed among surgical patients and included hemorrhage, venous thromboembolism, shock, transfusion, renal failure, respiratory failure, bacteremia, sepsis, pneumonia, other infection, and other complications.

Statistical analysis:

Retrieved citations were imported into EndNote X7 for duplicates removal. Subsequently, unique citations were imported into an Excel sheet and screened. The screening was conducted in two steps: title and abstract screening, followed by a full-texts screening of potentially eligible records. The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). P value < 0.05 was considered significant.

RESULTS

Among the 62,588 women identified with ectopic pregnancy, 49,090 (78.4%) underwent surgery with salpingectomy or salpingostomy, while 13,498 (21.6%) received medical management with methotrexate. As can be seen in figure (1), use of methotrexate increased significantly from 14.5% in 2011 to 27.3% by 2020 while surgical management declined from 85.5% to 72.7% over the same time period (P< 0.001).

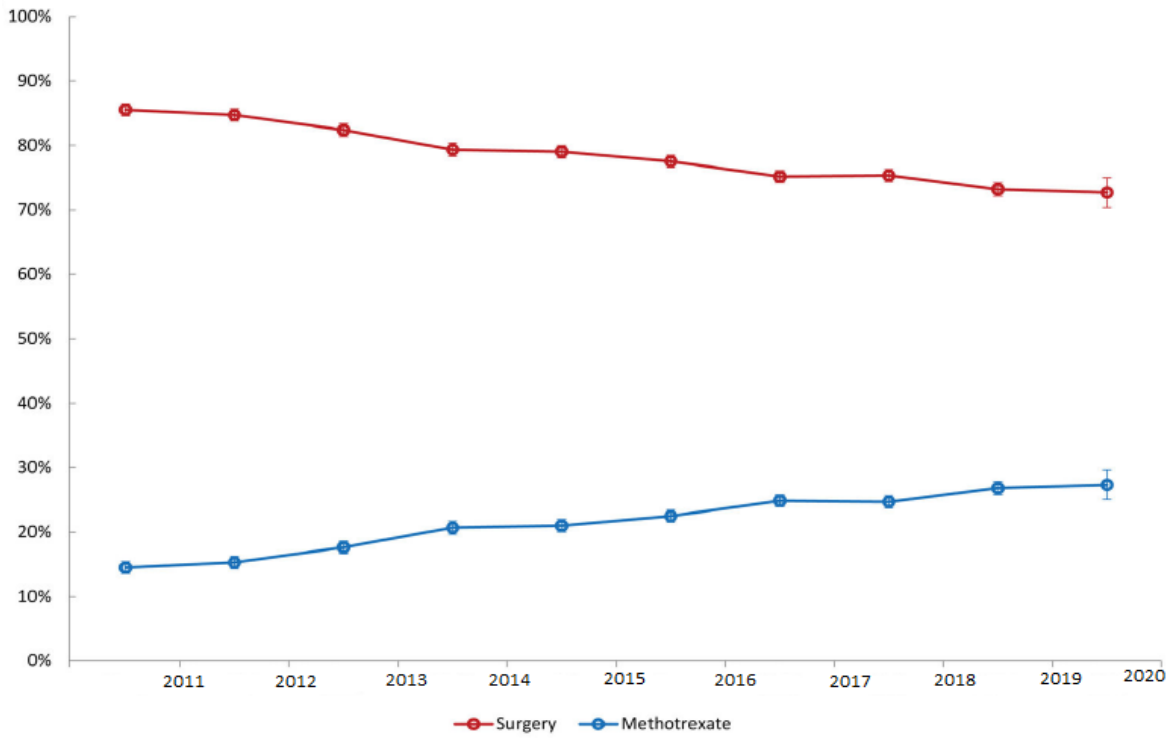

Figure (1): Medical versus surgical treatment

Among those women who underwent surgery, salpingostomy decreased over time from 13.0% in 2011 to 6.0% in 2020, while the rate of salpingectomy rose from 87.0% to 94.0% over the time period (P < 0.001) as shown in figure (2)

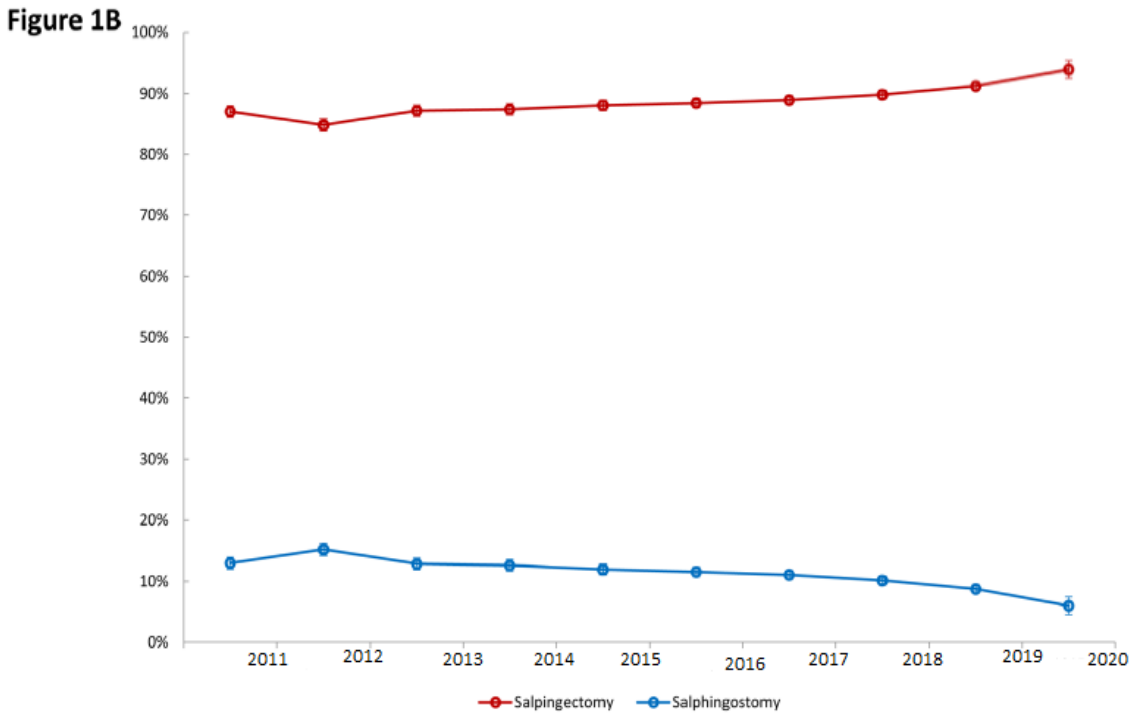

Figure (2): Salpingectomy versus salpingostomy.

Table (1) displayed the clinical and demographic characteristics of the cohort stratified by receipt of methotrexate or surgery. Treatment in more recent years, management at a teaching hospital and treatment at higher volume centers were associated with increased use of methotrexate (P<0.05 for all). Compared to women treated at a non-teaching facility, patients at teaching hospitals were 16% more likely to receive methotrexate (aRR=1.16; 95% CI, 1.02–1.33). In contrast, women with non-commercial insurance were less likely to receive methotrexate. Compared to women with commercial insurance, Medicaid recipients were 8% (aRR=0.92; 95% CI, 0.87–0.98) less likely and uninsured women 13% (aRR=0.87; 95% CI, 0.82–0.93) less likely to receive methotrexate.

Table (1): Clinical and demographic characteristics of the cohort stratified by methotrexate and surgery, and multivariable analysis of use of methotrexate

	Methotrexate		Surgery		P-value	Methotrexate aRR (95% CI)
	N	(%)	N	(%)		
All	13,498	21.6	49,090	78.4		
Age (years)					0.02	
<20	611	22.1	2,150	77.9		Referent
20-24	2,667	22	9,443	78		0.96 (0.89-1.04)
25-29	3,927	21.8	14,096	78.2		0.93 (0.87-1.01)
30-34	3,653	21.7	13,156	78.3		0.92 (0.85-0.99)*
35-39	2,048	20.4	7,977	79.6		0.88 (0.81-0.96)*
40-44	548	20.4	2,145	79.7		0.89 (0.80-1.00)*
≥45	44	26.4	123	73.7		1.20 (0.91-1.56)
Year					<0.001	
2011	784	14.5	4,626	85.5		Referent
2012	856	15.3	4,744	84.7		1.08 (0.97-1.19)
2013	1,034	17.6	4,837	82.4		1.24 (1.09-1.40)*
2014	1,252	20.7	4,805	79.3		1.46 (1.29-1.64)*
2015	1,405	21	5,291	79		1.48 (1.32-1.65)*
2016	1,749	22.5	6,034	77.5		1.57 (1.40-1.76)*
2017	2,110	24.8	6,383	75.2		1.73 (1.54-1.94)*
2018	1,974	24.7	6,030	75.3		1.72 (1.52-1.95)*
2019	1,932	26.8	5,271	73.2		1.89 (1.67-2.14)*
2020	402	27.3	1,069	72.7		1.97 (1.70-2.28)*
Marital status					<0.001	
Married	5,292	22.7	18,060	77.3		Referent
Single	6,665	21.4	24,471	78.6		0.98 (0.93-1.02)
Other/unknown	1,541	19	6,559	81		0.87 (0.77-0.99)*
Race					<0.001	
White	6,445	22.2	22,615	77.8		Referent
Black	3,369	21.3	12,448	78.7		0.96 (0.90-1.03)
Hispanic	729	19.4	3,024	80.6		1.00 (0.87-1.16)
Other/unknown	2,955	21.2	11,003	78.8		0.95 (0.88-1.03)
Insurance status					<0.001	
Commercial	6,800	23.1	22,680	76.9		Referent
Medicare	144	20.3	567	79.8		1.05 (0.90-1.22)
Medicaid	4,053	20.5	15,725	79.5		0.92 (0.87-0.98)*
Uninsured	2,044	19.9	8,245	80.1		0.87 (0.82-0.93)*
Unknown	457	19.6	1,873	80.4		0.87 (0.78-0.97)*
Hospital location					<0.001	
Urban	12,324	21.8	44,293	78.2		Referent
Rural	1,174	19.7	4,797	80.3		1.03 (0.88-1.22)
Hospital teaching status					<0.001	
Non-teaching	8,130	20.8	31,042	79.3		Referent
Teaching	5,368	22.9	18,048	77.1		1.16 (1.02-1.33)*
Hospital bed size					0.01	
<400	7,450	21.1	27,798	78.9		Referent
400-600	3,549	21.9	12,649	78.1		0.94 (0.81-1.08)
>600	2,499	22.4	8,643	77.6		0.84 (0.70-1.01)
Hospital region					<0.001	
Northeastern	1,817	20.6	7,011	79.4		Referent
Midwest	2,258	21.5	8,254	78.5		1.11 (0.90-1.36)
South	7,024	22.3	24,488	77.7		1.06 (0.88-1.27)
West	2,399	20.4	9,337	79.6		1.01 (0.82-1.23)
Comorbidity (Elixhauser)					<0.001	
0	12,322	24.6	37,802	75.4		Referent
1	947	9.9	8,602	90.1		0.41 (0.38-0.44)*
≥2	229	7.9	2,686	92.1		0.32 (0.28-0.37)*
Annualized hospital volume						
Median (IQR)	28 (18-43)		25 (15-37)		<0.001	1.010 (1.007-

* P-value <0.05

Older age, more recent year of treatment, the presence of medical comorbidities, non-white race, and non-commercial insurance coverage were all associated with a decreased likelihood of undergoing salpingostomy. Compared to white women, black (aRR=0.76; 95% CI, 0.69–0.85) and Hispanic (aRR=0.80; 95% CI, 0.66–0.96) patients were less likely to undergo tubal conserving surgery. Similarly, Medicaid recipients (aRR=0.69; 95% CI, 0.64–0.75) and uninsured women (aRR=0.60; 95% CI, 0.55–0.66) less frequently underwent salpingostomy than commercial insured patients. In contrast, compared to women residing in the Northeastern U.S., patients in the Midwest (aRR=1.51; 95% CI, 1.20–1.88) and West (aRR=1.62; 95% CI, 1.26–2.08) were more likely to undergo salpingostomy (Table 2).

Table (2): Clinical and demographic characteristics of surgery patients stratified by salpingostomy and salpingectomy, and multivariable analysis of predictors of salpingostomy

	Salpingostomy		Salpingectomy		P-value	Salpingostomy aRR (95% CI)
	N	(%)	N	(%)		
All	5,719	11.7	43,371	88.3		
Age (years)					<0.001	
<20	379	17.6	1,771	82.4		Referent
20-24	1,373	14.5	8,070	85.5		0.82 (0.74-0.90)*
25-29	1,770	12.6	12,326	87.4		0.66 (0.59-0.73)*
30-34	1,425	10.8	11,731	89.2		0.53 (0.48-0.59)*
35-39	682	8.6	7,295	91.5		0.42 (0.37-0.47)*
40-44	85	4	2,060	96		0.19 (0.15-0.25)*
≥45	5	4.1	118	95.9		0.19 (0.08-0.44)*
Year					<0.001	
2011	600	13	4,026	87		Referent
2012	721	15.2	4,023	84.8		1.16 (1.05-1.29)*
2013	621	12.8	4,216	87.2		1.00 (0.88-1.13)
2014	606	12.6	4,199	87.4		0.98 (0.87-1.11)
2015	632	11.9	4,659	88.1		0.96 (0.85-1.08)
2016	697	11.6	5,337	88.5		0.91 (0.81-1.03)
2017	706	11.1	5,677	88.9		0.86 (0.76-0.97)*
2018	612	10.2	5,418	89.9		0.81 (0.71-0.92)*
2019	460	8.7	4,811	91.3		0.72 (0.62-0.83)*
2020	64	6	1,005	94		0.51 (0.39-0.67)*
Marital status					<0.001	
Married	2,293	12.7	15,767	87.3		Referent
Single	2,751	11.2	21,720	88.8		0.92 (0.87-0.97)*
Other/unknown	675	10.3	5,884	89.7		0.90 (0.76-1.07)
Race					<0.001	
White	3,043	13.5	19,572	86.5		Referent
Black	1,068	8.6	11,380	91.4		0.76 (0.69-0.85)*
Hispanic	325	10.8	2,699	89.3		0.80 (0.66-0.96)*
Other/unknown	1,283	11.7	9,720	88.3		0.86 (0.77-0.96)*
Insurance status					<0.001	
Commercial	3,150	13.9	19,530	86.1		Referent
Medicare	49	8.6	518	91.4		0.70 (0.53-0.93)*
Medicaid	1,596	10.2	14,129	89.9		0.69 (0.64-0.75)*
Uninsured	722	8.8	7,523	91.2		0.60 (0.55-0.66)*
Unknown	202	10.8	1,671	89.2		0.74 (0.64-0.86)*
Hospital location					0.89	
Urban	5,163	11.7	39,130	88.3		Referent
Rural	556	11.6	4,241	88.4		0.94 (0.75-1.17)
Hospital teaching status					<0.001	
Non-teaching	3,797	12.2	27,245	87.8		Referent
Teaching	1,922	10.7	16,126	89.4		0.95 (0.79-1.15)
Hospital bed size					<0.001	

	Salpingostomy		Salpingectomy		P-value	Salpingostomy aRR (95% CI)
	N	(%)	N	(%)		
<400	3,409	12.3	24,389	87.7		Referent
400-600	1,453	11.5	11,196	88.5		0.91 (0.75-1.12)
>600	857	9.9	7,786	90.1		0.97 (0.75-1.25)
Hospital region					<0.001	
Northeastern	635	9.1	6,376	90.9		Referent
Midwest	1,215	14.7	7,039	85.3		1.51 (1.20-1.88)*
South	2,318	9.5	22,170	90.5		0.99 (0.79-1.24)
West	1,551	16.6	7,786	83.4		1.62 (1.26-2.08)*
Comorbidity (Elixhauser)					<0.001	
0	4,691	12.4	33,111	87.6		Referent
1	812	9.4	7,790	90.6		0.82 (0.76-0.88)*
≥2	216	8.0	2,470	92.0		0.76 (0.66-0.88)*
Annualized hospital volume						
Median (IQR)	25 (15-35)		25 (15-37)		0.02	1.001 (0.996-1.007)

* P-value <0.05

The overall perioperative complications rate was 23.4% (95% CI, 22.3–24.5%) among women who underwent salpingostomy and 34.9% (95% CI, 34.5–35.4%) after salpingectomy. Hemorrhage was the most frequent complication. In a multivariable model, complications remained 31% less common after salpingostomy (aRR=0.69; 95% CI 0.65–0.73). Older women were less likely than younger women to experience a complication, while Hispanic (compared to white) women (aRR=1.15; 95% CI 1.07–1.24), and uninsured patients (compared to commercial insurance) (aRR=1.12; 95% CI 1.07–1.17) were more likely to experience a complication (Table 3).

Table (3): Complications stratified by salpingostomy and salpingectomy among surgery patients

	Salpingostomy		Salpingectomy		P-value
	N	%	N	%	
All	5,719	11.7	43,371	88.3	
Any complications	1,337	23.4	15,150	34.9	<0.001
Hemorrhage	1,163	20.3	11,950	27.6	<0.001
VTE	1	0.02	13	0.03	0.6
Shock	32	0.6	1,199	2.8	<0.001
Transfusion	238	4.2	5,742	13.2	<0.001
Renal failure	1	0.02	68	0.2	0.01
Respiratory failure	15	0.3	277	0.6	<0.001
Bacteremia sepsis	1	0.02	41	0.1	0.06
Pneumonia	2	0.03	77	0.2	0.01
Other infection	11	0.2	253	0.6	<0.001
Other complications	113	2	1,474	3.4	<0.001

DISCUSSION

We noted substantial variation in the management of ectopic pregnancy in the U.S. While the rate of medical management with methotrexate is increasing among women who undergo surgery, tubal-conserving salpingostomy is being utilized less frequently. There are significant racial- and insurance-related disparities associated with treatment. First reported in 1985, medical management of ectopic pregnancy with methotrexate works via antagonism of the folic acid pathway in DNA replication, which impairs growth of the developing trophoblast [15, 16].

The optimal regimen of systemic methotrexate is debated, though data suggest that the single-dose

regimen is as effective as the multi-dose regimen and is associated with lower cost and fewer side effects [17]. Wider availability of methotrexate and use of early sonography have facilitated the growth in medical management, as also seen in other studies. When surgical management is selected, the decision of salpingostomy versus salpingectomy is often based on surgeon preference, patient history, and intraoperative appearance of the tubes, but when factoring in cost-effectiveness, recurrence risk, and future fertility, neither appears clearly superior [18].

Prior studies have shown that minority of women are not only at increased risk for the occurrence of ectopic pregnancy, but are also more likely to experience adverse outcomes. Among Medicaid recipients, the relative risk for ectopic pregnancy among black women was 1.26 compared to white women. Furthermore, the risk of death from ectopic pregnancy was 6.8 times higher for black women compared to white women. While more severe underlying pathology in underserved minorities may account for a portion of the variation in care that we noted, pathologic differences are unlikely to account for all of the variability we noted [19].

Regarding surgical versus non-surgical treatment of ectopic pregnancy, there is recent data promoting the benefits of tubal conservation to optimize future fertility without excessive risk of recurrent ectopic pregnancy. However, data are conflicting with regard to actual fertility outcomes in cases of tubal conservation, with some studies suggesting no difference in intrauterine pregnancy rates between conservative management and salpingectomy, but others reflecting significant improvement in fertility with conservative management. Concerning older age, more recent year of treatment, the presence of medical comorbidities, non-white race, and non-commercial insurance coverage were all associated with a decreased likelihood of undergoing salpingostomy. Compared to white women, black (aRR=0.76; 95% CI, 0.69–0.85) and Hispanic (aRR=0.80; 95% CI, 0.66–0.96) patients were less likely to undergo tubal conserving surgery. Similarly, Medicaid recipients (aRR=0.69; 95% CI, 0.64–0.75) and uninsured women (aRR=0.60; 95% CI, 0.55–0.66) less frequently underwent salpingostomy than commercial insured patients. In contrast, compared to women residing in the Northeastern U.S., patients in the Midwest (aRR=1.51; 95% CI, 1.20–1.88) and West (aRR=1.62; 95% CI, 1.26–2.08) were more likely to undergo salpingostomy.

Regarding laparoscopy versus laparotomy for treatment of tubal ectopic pregnancy, only one study gave a 'take home baby' rate [20]. This found a significantly higher 'take home baby' rate in the laparoscopically-treated group (38% vs. 22.2%), odds ratio (OR) 2.10 (95% CI, 1.27 – 3.47). Many studies gave intrauterine pregnancy rates and these were compared. No significant difference was observed in the intrauterine pregnancy rate between the two groups, combined OR 1.32 (95% CI, 0.58 – 3.02) [20, 21, 22, 23]. The studies reported ectopic rate per pregnancy. Three studies reported no significant difference in the ectopic rate per pregnancy in the two groups, combined OR 0.56 (95% CI, 0.18 – 1.73). In the studies, sufficient information was given to compare surgical techniques used at different stages of tubal disease [21, 22, 23]. Overall, there was no significant difference in the intrauterine pregnancy rate in treatment and control group for those patients with mild tubal disease, OR 1.06 (95% CI, 0.42 – 2.70). For patients with severe stage tubal disease, there was a significantly increased intrauterine pregnancy rate in the laparotomy group, OR 2.88 (95% CI, 1.16 – 7.16).

Regarding surgical treatment of ectopic pregnancy with salpingectomy versus salpingostomy, two randomized controlled trials and sixteen cohort studies were included. The largest of the two RCT's (69% of all subjects) enrolled only women with a normal contralateral tube whereas the cohort studies were more inclusive. In summary, in the RCT's there is no difference in outcomes between salpingectomies and salpingostomies for both subsequent IUP and REP. In the undifferentiated cohort studies salpingectomies are associated with a lower subsequent IUP rate and a lower subsequent REP rate, whereas in the cohort of women with risk factors, while salpingectomies still had a lower subsequent IUP rate they were associated with a higher REP rate.

Regarding efficacy and safety of expectant management in the treatment of tubal ectopic pregnancy, three studies reported on resolution of ectopic pregnancy (EP), the avoidance of surgery and time to resolution [24, 25, 26]. Only a single adverse outcome was reported in one patient in **Jurkovic *et al.*** [25], and none in **Silva *et al.*** [26]. Adverse events were reported in both the methotrexate and EM groups in **van Mello *et al.*** [24]. Health-related quality of life (HRQoL) was reported by **van Mello *et al.*** [27], and the abstract by **van Mello *et al.*** [24] reported on fertility outcomes. There were no identified RCTs that met criteria for the secondary outcome of patient preferences/experience. For the secondary outcome of whether surgery was avoided after the initial management strategy, there was insufficient evidence of a difference between expectant management (EM) and methotrexate (RR 1.10, 95% CI 0.94–1.29, P=0.25; I2 = 24%, two RCTs, 103 patients, low-certainty evidence). Only one adverse event was reported in one patient in the EM group of **Jurkovic *et al.*** [25] study who required a blood transfusion. As such, meta-analysis on adverse events was not possible. The average time to resolution of EP was reported by both studies, finding a mean difference of 3.0 days [25] and 1.4 days [26] with insufficient evidence of benefit for methotrexate (pooled mean difference = _2.56, 95% CI _7.93–2.80, P=0.35; I2 = 0, two RCTs, 103 patients, low-certainty evidence).

CONCLUSION

Ectopic pregnancies account for the majority of first trimester maternal death. Tubal pregnancies account for the majority of ectopic pregnancies. There was difference in health care delivery systems for the treatment of ectopic pregnancy. Further investigation to better understand the mechanisms underlying the disparities we noted is needed.

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