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Developing A Hospital Specific and Evidence-Based Management Protocol for Pregnancies of Unknown Location and Ectopic Pregnancies: A Retrospective Chart Review and Quality Improvement Project

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Introduction

An ectopic pregnancy is defined as a pregnancy that occurs outside of the uterine cavity. Ectopic pregnancies (EP) account for 2% of all pregnancies and are the leading cause of morbidity and mortality in the first trimester [1]. Women presenting to the emergency room with vaginal bleeding and/or abdominal pain have been shown to have a prevalence of EP as high as 18% [2]. When a woman presents with a positive urine pregnancy test early in pregnancy it is not uncommon that an ultrasound is unable to visualize the location of the pregnancy, and therefore an EP cannot be excluded. This is known as a pregnancy of unknown location (PUL) and is a temporary diagnosis that requires close follow up until a final diagnosis can be made. Follow up often includes serial beta-HCG levels as well as additional ultrasounds. Final diagnoses most commonly include early viable pregnancy, ectopic pregnancy, and failed intrauterine pregnancy. In order to reduce the potential for morbidity and mortality, EP must remain high on the differential of diagnosis in the setting of PUL.

At Regional One Health (ROH) in Memphis, TN, patients with PUL or EP are managed based on a protocol until a final diagnosis has been reached. ROH is unique in that Women's services includes both a Labor and Delivery as well as an Obstetrical Emergency Department (OB ED) where pregnant women can receive 24/7 emergency room care. The current practice for PUL and EP at ROH is to have patients follow up in the OB ED, even if non-emergent. The cost of care provided in an emergency room setting has been shown to be significantly more expensive than the equivalent care when given in a clinic setting [3] and therefore the current recommended management is most likely creating a financial burden both for our patients and our hospital. In addition, the current management protocol was approved in 2012 and has not been updated with the most recent evidence-based recommendations for management of PUL, leading to discrepancies in management and confusion among providers in how to adequately care for these patients.

In 2007 the Institute for Health Care Improvement developed a framework for optimizing healthcare performance known as the Triple Aim, which encouraged health care institutions to pursue improving three dimensions: population health, the patient's experience of care, and per capita costs. Improving and updating the PUL protocol at ROH is a necessary step to achieving the triple aim for healthcare improvement and reducing morbidity and mortality for our patients. The objective of this study was to evaluate current practices in the care of women with PUL and EP in order to analyze risk factors, identify systemic inefficiencies in care, and create an updated and evidence-based protocol for the management of these patients in order to improve patient care and per capita healthcare costs.

Methods

Approval for this study was first obtained from the Institutional Review Board of the University of Tennessee Health Sciences Center (UTHSC) and the Office of Medical Research at Regional One Health. A retrospective chart review of women followed by the UTHSC OBGYN "Ectopic List" from April to October of 2019 was completed. The UTHSC OBGYN residents use an internal patient tracking system called eDocList for patients in Memphis with PUL and EP. Past chart reviews of ectopic pregnancies at ROH were limited by paper medical records and for this reason the

date range was chosen to include the first six months of patient care with the new unified electronic medical record (EMR). eDocList was reviewed within the given time frame and all patients with encounters at ROH during the study time frame underwent chart review. Patients were excluded if they had no information in the ROH EMR or if they were given a final diagnosis prior to the study time frame. Patient charts were then reviewed.

Information collected during chart review included age, race/ethnicity, BMI, gravity, parity, risk factors for ectopic pregnancy, gestational age at initial presentation, presenting symptoms, initial diagnosis, and final diagnosis. The number of emergency room visits, lab only visits, and clinic visits were also tabulated. This data was analyzed by the UTHSC Biostatistics, Epidemiology, and Research Design Group for demographic and clinical variables as well as risk factors of ectopic pregnancy. Demographic and clinical variables were summarized descriptively. Univariate odds ratios with confidence intervals and p-values predicting ectopic pregnancies (ruptured or non-ruptured) were determined using logistic regression modeling. All statistical calculations were performed using R version 3.5.1. Variables which did not have cases of both ectopic and non-ectopic pregnancies were excluded. Beta-HCG lab values, ultrasound results, and treatments given were recorded and based on this information a comparative analysis was completed to assess if the current management protocol had been properly followed and if not, why.

A qualitative review of patient encounters was then performed in order to identify and summarize systemic inefficiencies in care. A literature review on management of pregnancies of unknown location as well as ectopic pregnancies was completed. Based on this literature review as well as the data analysis from ROH an updated evidence-based and hospital specific protocol was developed for patients with PUL or EPs.

Results

Initially, 90 patients were identified from the eDocList from April to October of 2019, and, 73 met inclusion criteria for chart review (16 patients were excluded due to having no encounters at ROH; 1 patient was excluded because a final diagnosis was reached prior to the study time frame). Patient demographics and baseline encounter information are shown in Table 1. Patients had an average of 2.53 [0-11] ED visits, 0.43 [0-8] laboratory visits, and 0.40 [0-3] clinic visits. During these visits, patients underwent an average number of 2.93 [0-12] HCG blood draws and 1.73 [0-7] ultrasounds.

The initial and final diagnoses of patients in the study are shown in Table 2. Ectopic pregnancy was diagnosed in 21 (28.8%) patients, intrauterine pregnancy in 16 (21.9%) patients, failed pregnancy in 23 (31.5%) patients, molar pregnancy in 2 (2.7%) patients. Additionally, 11 (15.1%) patients were lost to follow-up prior to receiving a final diagnosis, and 21 (28.8%) patients were lost to follow-up prior to completing the recommended care. Of the 58 patients who initially presented with PUL, 11 (19.0%) had a final diagnosis of ectopic pregnancy. Box 1 demonstrates the distribution of the patients studied as well as the final diagnoses given to patients initially found to have PUL.

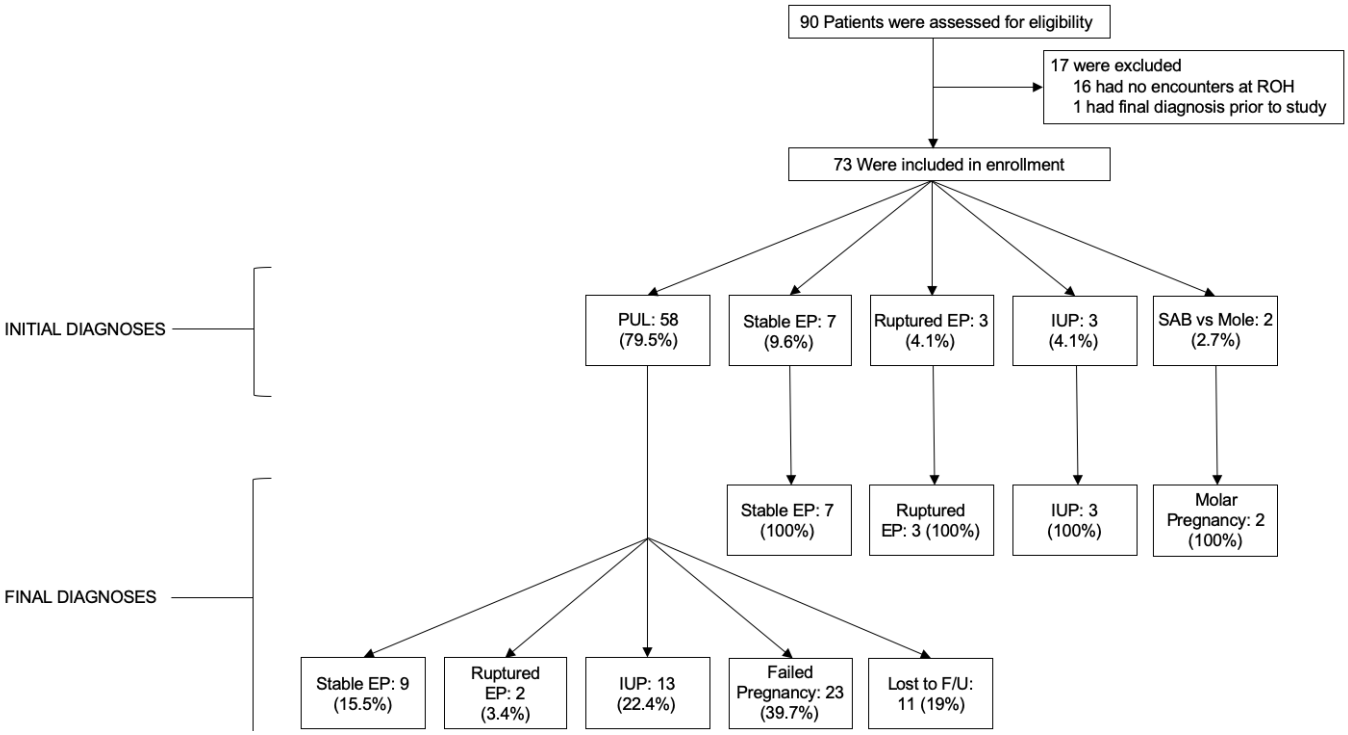
	Mean	Median [min-max]
Age	26.40	25 [14-39]
BMI	29.10	27 [18-53]
Gravida	3.54	3 [0-17]
Parity	1.53	1 [0-8]
Presenting Gestational Age	6.00	5.5 [5-12.0]
Race/Ethnicity:	Total	%
Black/AA	52	71.2%
White	9	12.3%
Hispanic/Latino	6	8.2%
American Indian/Alaskan Native	1	1.4%
Asian	1	1.4%
Unknown	4	5.5%
	Mean	Median [min-max]
# HCGs	2.93	2 [0-12]
# USG	1.73	1 [0-7]
Resident USG	0.56	0 [0-4]
Formal USG	1.18	1 [0-4]
ROH ED visits	2.53	2 [0-11]
Lab visits	0.43	0 [0-8]
Clinic visits	0.40	0 [0-3]

Table 1: Patient demographics and baseline encounter information.

Initial Diagnosis	Total	% of total patients
PUL	58	79.5%
Stable EP	7	9.6%
Ruptured EP	3	4.1%
IUP	3	4.1%
Molar Pregnancy	1	1.4%
SAB vs. Molar pregnancy	1	1.4%
Final Diagnosis		
Ectopic Pregnancy	21	28.77%
Intrauterine Pregnancy	16	21.92%
Failed Pregnancy	23	31.51%
Molar Pregnancy	2	2.74%
Lost to Follow Up	11	15.07%

Table 2: Initial and final diagnoses.

The presenting symptoms and additional risk factors are shown in Table 3. In prior epidemiological studies and meta-analysis [2,4]



Box 1: Initial and final diagnoses.

significant risk factors for ectopic pregnancy include history of ectopic pregnancy, history of pelvic inflammatory disease, history of infertility, prior pelvic/tubal surgery, assisted reproductive therapy. Less significant risk factors include cigarette smoking, and age >35 years old. In this study, 29 (39.73%) patients were found to have recorded risk factors. Of the 21 patients with a final diagnosis of ectopic pregnancy, 8 (38.1%) had documented risk factors compared to 16 (39.0%) of the 41 patients with a final diagnosis that was not ectopic pregnancy. Of the 21 patients with ectopic pregnancy, 13 (61.9%) patients had no risk factors documented. Of the 73 total patients 0 had a recorded history of PID, ART, or infertility. Only 6 patients had a recorded history of STDs. A clinical scenario that commonly presents is an initial ultrasound that reveals abnormal adnexa but no definitive EP. Of note, 29 (39.7%) patients had an initial ultrasound with abnormal adnexa that could not rule out ectopic pregnancy. Of these 29 patients, 13 (44.8%) had ectopic pregnancies, 12 (41.4%) had either viable or failed intrauterine pregnancies, and 4 (13.8%) were lost to follow-up prior to a final diagnosis.

Odds ratios for demographic and clinical characteristics for all patients were calculated and are shown in Table 4. Initial ultrasound with adnexal findings showed a statistically significant predisposition for EP with an OR of 3.93 (CI 1.33-12.38, P=0.0156). A later gestational age at presentation was also found to be statistically significant for EP with an OR of 1.06 (CI 1.00-1.12, P=0.0474). No patients with a history of STDs were found to have ectopic pregnancies. Age ≥35 and history of prior pelvic surgery were found to increase a patient's odds of having an ectopic pregnancy; however, this was not found to be statistically significant. BMI, History of EP, cigarette smoking, and history of cesarean section, were all found to have an odds ratio <1.0 and were not statistically significant.

Beta-HCG lab values, ultrasound results, and treatments given were analyzed to assess if the current management protocol had been properly followed and if not, why. Management did not follow the protocol for 61 (83.56%) patients. These results are shown in Table 5. In 20 (27.4%) cases the protocol was not followed due to patient factors such as loss to follow-up, leaving against medical advice, or desiring continued expectant management. 13 (17.8%) patients did not undergo a diagnostic dilation and curettage as indicated by the protocol, 1 of which resulted in a final diagnosis of an intrauterine pregnancy. Additionally, 6 (8.22%) patients had a clinical course that behaved such that the protocol was inadequate and could therefore not be followed.

As a component of the retrospective chart review recurrent inefficiencies and inconsistencies in patient care were identified and are listed in Box 2. Issues that will directly increase cost to the healthcare system and the patient include use of the OB Emergency Department for non-emergent care, and patients leaving against medical advice or without being seen. The issues shown in Box 2 were considered when developing the new management protocol.

Presenting symptoms (N=73)	Total	% (of N)
Abdominal Pain & Vaginal Bleeding	16	21.92%
Vaginal Bleeding	30	41.10%
Abdominal Pain	19	26.03%
Other	3	6.85%
None Documented	5	5.48%
Recorded Risk Factors (N=73)		
Total Patients with Any Risk Factors	29	39.73%
Significant risk factors		
History of EP	11	15.1%
History of Pelvic surgery	14	19.2%
History of PID, ART, or Infertility	0	0%
Less Significant risk factors		
Smoker	15	20.5%
Age >35	10	13.7%
History of STDs	6	8.2%
Recorded Risk Factors of Patients with EP (N=21)		
Total Patients with Any Risk Factors	8	38.1%
Significant risk factors		
History of EP	3	14.29%
History of Pelvic surgery	6	28.57%
History of PID, ART, or Infertility	0	0%
Less Significant risk factors		
Smoker	3	14.29%
Age >35	4	19.05%
History of STDs	0	0%
No Recorded Risk Factors	13	69.10%
Initial Ultrasound with Adnexal findings (N=73)		
Total	29	39.73%
Final Diagnosis: EP	13	44.8%
Final Diagnosis: IUP	5	17.2%
Final Diagnosis: Failed Pregnancy	7	24.1%
Lost to Follow up	4	13.8%

Table 3: Presenting symptoms and risk factors.

Variable	Odds Ratio	95% CI	p-value
Age	1.03	0.94-1.12	0.5564
BMI	0.97	0.90-1.04	0.4338
Gestational Age at presentation	1.06	1.00-1.12	0.0474
History of Ectopic Pregnancy	0.83	0.16-3.42	0.8067
History of pelvic surgery	2.02	0.56-7.20	0.2728
Cigarette smoker	0.53	0.11-2.02	0.3803
Age ≥ 35	1.75	0.39-7.49	0.4468
History of C-section	0.61	0.12-2.36	0.4963
Initial ultrasound with adnexal findings	3.93	1.33-12.38	0.0156

Table 4: Odds Ratios of risk factors.

	Total	% of total
Protocol Not Followed	61.00	83.56%
No progesterone	54.00	73.97%
No Diagnostic D&C	13.00	17.81%
Patient factors	20.00	27.40%
Rpt USG <2000 HCG	4.00	5.48%
No 48hr f/u for declining HCG	7.00	9.59%
Inadequate protocol	6.00	8.22%

Table 5: Adherence to current protocol.

Box 2. Common issues associated with care of patients with PUL and EP at ROH

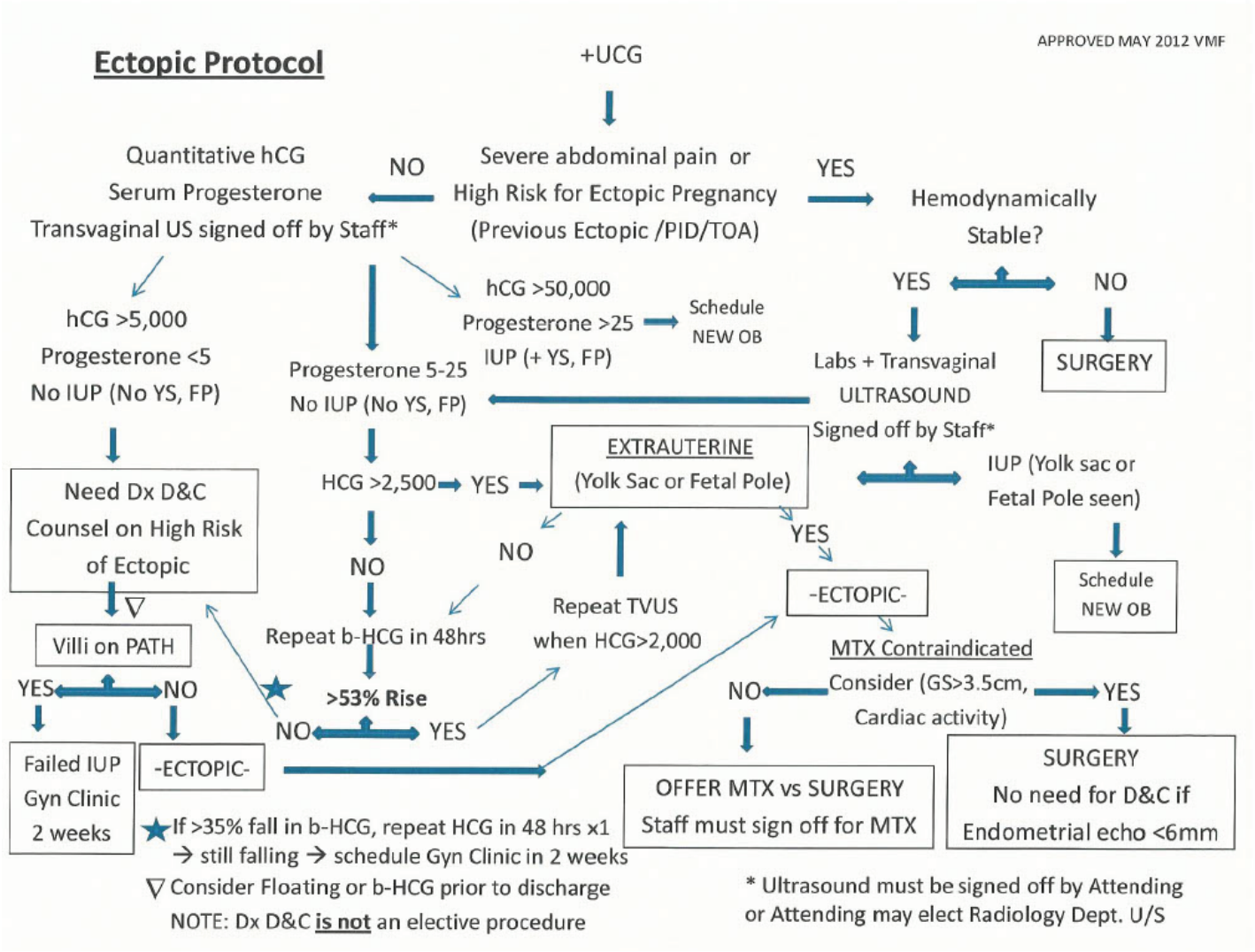
- Use of the OB Emergency Department for non-emergent care
- Prolonged continuation of "strongly desired" failed pregnancies
- Patients leaving against medical advice, without being seen, not following up as recommended, or declining treatment
- Inadequate or no documentation of reminder calls made to patients
- Variable follow-up after surgical management
- Inconsistent documentation of a negative pregnancy test after care
- Patients with established OBGYNs outside of ROH
- Inconsistent progesterone levels ordered
- Difficulty making clinic appointments or lab visits
- Inadequate review of previous records

Management Protocol for Pregnancies of Unknown Location and Ectopic Pregnancies

A new protocol was developed based on a review of the current literature and the findings described above. The current protocol is shown in Box 3 and the proposed updated protocol is shown in Box 4. The current protocol does not specify the location of follow up which has resulted in most care being given in the OB ED. The updated protocol now has specifications of where follow up is intended to occur. All follow up HCG visits have been redirected to the clinic setting as a lab visit and follow up ultrasounds have also been redirected to the clinic. Based on specific increases or decreases in HCG levels obtained from the literature, specific management pathways have been outlined. Given that an initial ultrasound with adnexal findings was found to be a statistically significant predisposing factor for EP, this was added as a separate pathway in the protocol with heightened monitoring. As a component of the protocol, it is written that care may be redirected to the OB ED if a patient develops a concerning change in symptoms. It also emphasizes the importance of documenting thoroughly as well as redirecting care to a patient's primary OBGYN if applicable.

Discussion

This study indicates that, within the given patient population and time frame, minimal conclusions can be reached regarding patient risk factors at initial presentation that can predict their risk for ectopic pregnancy. Adnexal findings at initial ultrasound was shown to be a statistically significant predictor of EP. Gestational age was also found to be a statistically significant predictor however this is likely a weakly predictive factor as the lower confidence interval is 1.00. In looking at these patient encounters,

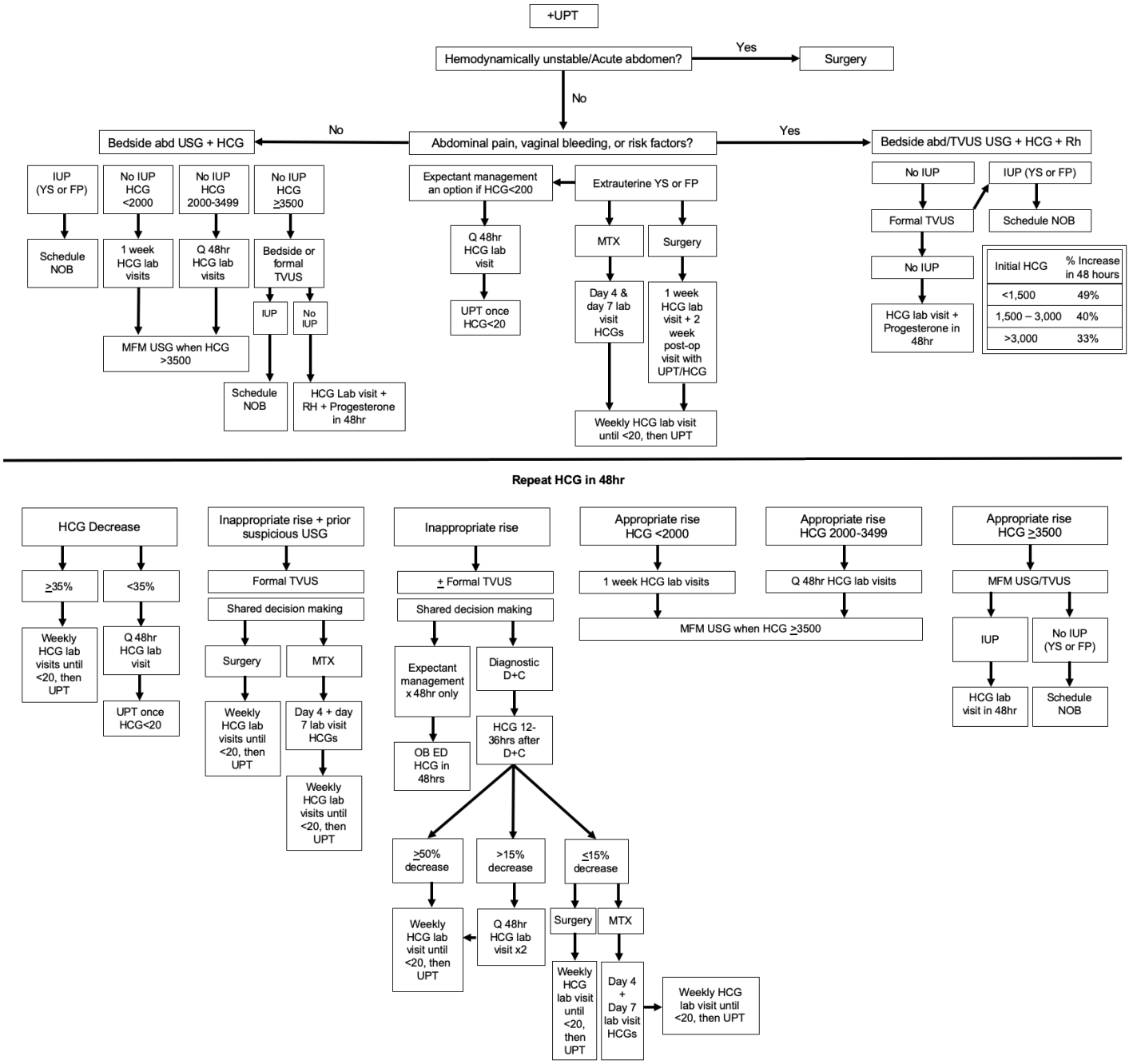


Box 3: Current Regional One Health "Ectopic Protocol"

however, we can conclude that the current protocol at Regional One Health is insufficient in guiding the care of patients with PUL or EP and this has led to inconsistencies and inefficiencies in the care of these patients, poor patient compliance, as well as unnecessary emergency room visits at an increased cost to the health care system. By taking into account the findings from this study as well as the current body of literature related to the management of PUL and EP, the protocol developed is anticipated to show an improvement in the management of these patients, both by reducing emergency room visits and streamlining care for patients and providers.

Results from the patients included in this study are largely inconsistent with the existing literature in that known risk factors such as history of prior ectopic pregnancy were found to be 27% (OR 0.83) less likely to have an EP. These results were not statistically significant and were limited by a small population size. A larger sample size might have resulted in data more consistent with the literature. The data does demonstrate the need for an updated protocol as the current protocol is out of date and was rarely followed.

When considering the common issues identified in the care of patients with PUL and EP at ROH, many practical solutions can be drawn from this information. It would likely be beneficial for the new protocol to be rolled out in conjunction with an educational component that reviews treatment of ectopic pregnancy, diagnosis and treatment of failed pregnancies, counseling of patients on precautions and recommendations, as well as adequate documentation. An effort needs to be made to ensure that patients are reconnected with their primary OBGYNs when possible, as this will improve continuity of care, patient satisfaction and compliance. Difficulty, on the part of the clinic staff, scheduling clinical appointments and timely laboratory visits was also noted, however this may have been due to the use of a new EMR. The new revised protocol redirects visit to the clinic setting and therefore scheduling lab visits and clinic appointments will need to be done in a timely fashion.



- ❑ Ectopic and bleeding precautions given at all encounters and follow-up phone calls
- ❑ Assess for hemodynamic instability and acute abdomen at all OB ED encounters
- ❑ Appointment reminder calls for all follow-ups: Assess for symptoms, can redirect to ED if necessary
- ❑ If symptoms are severe and ED follow-up is warranted, document well
- ❑ If patient has non-ROH primary OB: call clinic to confirm follow-up appointment, document, remove from eDocList

Box 4: Proposed updated protocol for pregnancies of unknown location and ectopic pregnancies [5-14]

Limitations

Analysis of odds ratios was limited due to small numbers in the given time frame as well as many patients being lost to follow up prior to a final diagnosis. Eligible patients were found using eDocList which is an internal tracking list that is not conducive to research or data extraction. Retrospective patient identification from the eDocList was performed manually and was therefore subject to human error and omission of potentially eligible patients. It is also possible that not all patients with PUL or EP seen at ROH were added to the eDocList, as this is also performed manually and is subject to human error. Documentation in the EMR was also a large limitation of this study. Patient risk factors were often inadequately documented as well as other clinical data. Lastly, the qualitative review of systemic inefficiencies and issues was conducted by the researcher, a resident physician, and was often a subjective rather than objective assessment based on the researchers own experience and biases in executing the current protocol and managing this patient population.

Conclusions

In order to adequately address the IHI triple aim of improving the patient experience, population health, and per capita cost, an updated evidence-based and hospital specific management protocol is necessary. Frequent emergency room visits, long wait times, and inconsistent care have led to difficulties with patient compliance. Poor compliance and follow up among patients can be indicative of poor understanding of the clinical scenario, poor communication of recommendations given, and socioeconomic challenges. In conclusion, the updated protocol for managing patients with PUL and EP aimed to improve patient and provider satisfaction as well as cutting healthcare costs. In order to improve the data analysis from this study it may be beneficial to expand the time frame and review a larger number of patients. Moving forward, the new protocol will need to be reviewed and approved by the UTHSC OBGYN department, and an educational component will need to be developed and implemented in order to educate staff on the new process. After the implementation of the new protocol it will be possible to repeat an analysis of patients with PUL and EP and examine whether the new protocol leads to increased compliance and reductions in ED visits and therefore costs.

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