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CLINICAL REVIEWS

Frequency of utilisation of ultrasound in the diagnosis of ectopic pregnancy in Sub-Saharan Africa countries: A systematic review



Fréquence du recours à l'échographie dans le diagnostic des grossesses ectopiques en Afrique subsaharienne: Analyse systématique

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Introduction: Ectopic pregnancy (EP) is a common diagnosis, frequently misdiagnosed early in its presentation and a leading cause of first trimester mortality. Ultrasound (US) is a key component of evidence-based diagnostic algorithms. We present a systematic review on the frequency of the use of US in the diagnosis of EP in Sub-Saharan Africa.

Methods: A librarian-assisted search of PUBMED, EMBASE, Cochrane, Web of Science, and POPLINE databases was performed. Inclusion criteria were original research studies that reported the proportion of patients receiving US as part of a workup for EP in a Sub-Saharan African country. Abstracts were reviewed and those potentially meeting criteria had a formal survey of the manuscript.

Results: The initial search revealed 784 original publications. Manual review of abstracts narrowed this to 91 papers with potential relevance, and 12 studies were included in the final analysis. A total of 6055 patients diagnosed with EP were included. 8.7% received a pregnancy test. 92.3% were ruptured at the time of presentation. 42.9% were in shock and 75.8% received red blood cell transfusion. 73.7% were unaware of the pregnancy and 24.9% were seen by a healthcare worker prior to presentation, 1.1% of patients died. Overall, 12.6% received US to aid in the diagnosis.

Conclusion: In this study, overall utilisation of US in the diagnosis of EP was found to be low. In this population, patients presented late and critically ill, obviating the need for US in many cases. However, studies in Sub-Saharan Africa in populations of patients with similar rates of late presentations have shown a substantial increase in the diagnosis of unruptured EP with the routine use of US.

Introduction: La grossesse ectopique (GE) est un diagnostic courant, faisant fréquemment l'objet d'erreurs de diagnostic précoces lors de la consultation, et l'une des principales causes de mortalité au cours du premier trimestre. L'échographie est une composante clé des algorithmes de diagnostic scientifiquement fondé. Nous présentons ici une analyse systématique du recours à l'échographie dans le diagnostic de la GE en Afrique subsaharienne.

Méthodes: Une recherche dans les bases de données PUBMED, EMBASE, POPLINE, Cochrane et Web of Science, assistée par un bibliothécaire, a été réalisée. Les critères d'inclusion étaient des études scientifiques originales faisant état de la proportion de patientes faisant l'objet d'une échographie dans le cadre d'un bilan sur la GE dans un pays d'Afrique subsaharienne. Les résumés ont été consultés, et les articles susceptibles de répondre aux critères ont fait l'objet d'un examen détaillé.

Résultats: L'étude initiale a identifié 784 publications originales. L'examen manuel des résumés a permis de réduire ce chiffre à 91 articles susceptibles d'être pertinents, et 12 études ont été incluses à l'analyse finale. Au total, 6 055 patientes diagnostiquées comme souffrant d'une GE ont été incluses. 8,7 % se sont vues administrer un test de grossesse. 92,3 % souffraient d'une grossesse rompue au moment de la consultation. 42,9 % étaient en état de choc et 75,8 % ont reçu une transfusion de globules rouges. 73,7 % n'étaient pas conscientes de la grossesse, et 24,9 % en avaient été informées par un agent de santé avant la consultation. 1,1 % des patientes sont décédées. Au total, 12,6 % ont passé une échographie en appui au diagnostic.

Conclusion: Dans cette étude, le recours général à l'échographie pour diagnostiquer une GE était faible. Dans cette population, les patientes consultaient tardivement et en état critique, éliminant la nécessité d'un recours à l'échographie dans nombre de cas. Cependant, des études menées en Afrique subsaharienne auprès de populations de patientes présentant des taux de consultation tardive similaires ont indiqué une augmentation substantielle du diagnostic de GE sans rupture grâce au recours systématique à l'échographie.

African relevance

- Prevalence of ectopic pregnancy is approximately 1–5% in Sub-Saharan hospital based studies, consistent with what is seen in other parts of the world.
- Reported mortality rates for ectopic pregnancy are much higher in Sub-Saharan African countries than those seen in the United States and the United Kingdom.

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- Clinical algorithms incorporating the use of ultrasound for early diagnosis of ectopic pregnancy have improved early detection and contributed to the decline in ectopic pregnancy mortality in low to middle income countries.

Introduction

Ectopic pregnancy (EP) accounts for more than three quarters of early maternal deaths in the United States and the United Kingdom and is responsible for 9–17% of all maternal deaths in these countries.^{1,2} Worldwide, it is a leading cause of first trimester maternal deaths.³

Hospital-based studies in Sub-Saharan Africa (SSA) have reported the incidence of EP to be between 1.1% and 4.6% of pregnancies,^{2,4} reflecting a fourfold increase between 1977 and 1994.⁴ By comparison, EP occurs in 1.5–2.0% of pregnancies in the United States, where the incidence increased by a factor of six between 1970 and 1992 but has remained stable since.⁴ Direct costs of treating EP are estimated at \$1 billion USD in the United States alone.¹

Additionally, hospital-based studies in SSA report high mortality rates, ranging between 1% and 3%.² These are likely underestimates, as many cases go unreported or misclassified because they are recorded in female wards rather than maternity wards, and deaths occurring outside of health facilities are generally excluded from health services data in the region.^{2,3} In contrast, high-resource settings report that mortality from EP has fallen dramatically in recent decades, from 35.5 to 3.8 deaths per 10,000 women between 1970 and 1989 in the United States, and from 16 to 3 deaths per 10,000 pregnancies between 1973 and 1993 in the United Kingdom.¹ Mortality from EP in the United States is currently 0.05%.⁴

Clinical algorithms requiring ultrasound (US) for early diagnosis of EP have improved early detection and contributed to the decline in EP mortality in developed countries.^{1,2,4–6} There is limited data on how frequently US is being used to evaluate EP in SSA. We performed a systematic review of the literature in order to assess the utilisation of US, when available, in the diagnostic work-up of EP in countries in SSA.

Methods

The design and results of this systematic review conform to the recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).⁷ This study did not meet the criteria for human subjects research requiring review by the Committee on Human Research at the University of California, San Francisco.

A comprehensive librarian-assisted literature search was performed of PubMed, EMBASE, Cochrane, POPLINE, and Web of Science. The literature search retrieved citations from database inception to June 25, 2012 in all languages and was limited to human subjects. The search terms included “ectopic pregnancy”, “maternal haemorrhage”, and “Sub-Saharan Africa”. We did not include “ultrasound” because we wanted to catch all papers that reported on the work up of ectopic pregnancy even if they were not US focused. The full terms of the search are available on request from the

corresponding author. Bibliographies of articles identified through electronic searches were further reviewed for additional studies not previously recognised.

One author (AF) reviewed all of the titles and abstracts included by the search. All English language titles or abstracts assessed to be potentially relevant were eligible for further formal review of the full article. If full text articles were not available in English, they were excluded. Three authors (AF, SK, and TR) then independently reviewed all potentially relevant articles for inclusion based on the following criteria; disagreements were resolved by consensus discussion and all three reviewers agreed on the final list.

We included original research studies that (1) reported that US was available and (2) reported on the frequency of the US use in the evaluation of patients at risk of ectopic pregnancy. We excluded studies if they: (1) were case reports, or (2) reported availability of US but did not report frequency of use.

Data were extracted from the included studies using a standardised abstraction form. Epidemiological information extracted included study type, type of hospital, location, age, marital status, education level, parity, and urban or rural residence. Relevant aspects of medical history, including prior ectopic pregnancy, abdominal surgery, pelvic inflammatory disease (PID), or sexually transmitted infection (STI) were abstracted. Clinical characteristics extracted included frequency of the use of US and pregnancy testing, patient awareness of pregnancy, previous patient evaluation by healthcare worker, number of patients that had ruptured EP on presentation, and number that were in shock or required blood transfusions. The author of one article was emailed for clarification of a data discrepancy regarding a percentage miscalculation, but did not respond.

Data were aggregated when feasible and descriptive statistics were reported as rates or percentages. Some variables (age, parity) were made categorical based on the available data reported, and others (blood transfusion) were made binary. Data were entered in an Excel Spreadsheet (Microsoft Excel for Mac Version 12.3, Redmond, Washington) and descriptive statistical calculations were performed.

Results

The initial database search strategy yielded 784 non-duplicate studies (Fig. 1). Title and abstract review yielded 91 articles with potential relevance. The full articles for the potentially relevant studies were reviewed and 12 studies were identified for abstraction of data for epidemiological analysis.^{8–18}

Patient demographics are reported in Table 1. Mean patient age was 25.6 years, with 83.1% of patients between 20 and 34 years. Overall, 77.4% had been pregnant at least once before and over half were married. 73% had less than a secondary education, which was defined as less than six years of formal education. Location of patient residence was nearly equal between rural (41.3%) and urban (50.6%), with some patients living in both rural and urban areas. Unexpectedly, few patients had a history of known risk factors such as previous abdominal or pelvic surgery (4.4%), previous EP (6.8%), or history of STI or PID (8.4%).

All 12 studies reported frequency of US use in the diagnosis of EP (Table 2). A total of 761 ultrasounds were performed in 6055 patients (12.6%). Rarely was a differentiation made

whether patients received transabdominal US or transvaginal US. Frequently, diagnostic procedures including paracentesis, culdocentesis, and laparoscopy were used in addition to or in place of US in the diagnostic work-up. In unstable patients with a high index of suspicion, diagnostic or therapeutic laparotomy was often performed without the aid of less invasive methods for diagnosis.

Ten studies reported on the EP rate. EP rate ranged from 0.27% to 4.09% of deliveries and on pooled analysis, 5781 EPs were reported over a time period when 347,114 deliveries were performed, for an overall EP rate of 1.67% of all deliveries reported.

Eight studies reported on whether the patient presented in shock, defined by unstable cardiovascular vital signs such as hypotension (SBP < 90) with tachycardia (HR > 100). 1031 patients presented in shock from a group of 2406 patients with EP, for a rate of 42.9%. Five studies reported on the use of blood products, with 75.8% patients receiving at least one unit of red blood cells.

Eleven studies reported on the rate of EPs that were ruptured on arrival to the hospital. Overall, 92.3% were ruptured on arrival. Two studies reported that 24.9% of patients were evaluated at another healthcare facility prior to arrival at the hospital. In reports from 7 studies, only 8.7% of patients presenting with EP had pregnancy tests before or in the hospital. 73.7% of patients did not know they were pregnant prior to presentation for EP. Overall the case fatality rate, reported in 11 studies, was 1.1%.

This population is not a representative sample. It is a convenience sample of populations described in published hospital-based studies and is subject to reporting bias. In addition, it is not known whether the rate of US use in facilities included in this sample is similar to that of hospitals in the region overall.

Although we report an overall mean of 12.6% use of US in SSA, this is an oversimplification of the data. With some centres reporting upwards of 80% and others reporting as low as 4%, reporting an overall utilisation proportion could lead one to assume that US use is more homogenous than we believe it to be.

Hospital-based studies may also lead to a selection bias towards a population with higher severity of illness than those seen at primary care clinics or not seen at all. There is a lack of population-based data to inform our understanding of the true incidence of EP and its associated mortality rate in SSA.³ In addition, seven of the 12 included studies were retrospective

chart reviews, which are subject to the potential inaccuracies of written records and missing important data.

Discussion

Mortality rate for EP towards the end of the 19th century was 72–99%. Between 1908 and 1947, mortality rates dropped from 12.3% to 1.7–2.7% with earlier diagnosis with the use of culdocentesis and pregnancy testing, as well as with the adoption of laparoscopic diagnosis and treatment.¹⁹ But even in the mid-twentieth century, when the successful surgical management of EP was celebrated as “an outstanding obstetric and gynaecological achievement”, 20% of preoperative diagnoses of EP were found to be wrong intra-operatively, and 20% of all EPs diagnosed intra-operatively had gone to the operating room for a different presumed diagnosis. Diagnosis of unruptured EP was thought to be nearly impossible.¹⁹

Ultrasonography was shown to improve diagnostic accuracy of EP as early as the 1960s, and algorithms combining US with rapidly improving hCG testing have become the diagnostic standard of care over the past 50 years, a revolution that “chang(ed) the diagnosis of unruptured ectopic pregnancy from impossible to feasible to even mandatory, shifting the aim of therapy from reduction of mortality to preservation of future fertility.”¹⁹

Our results suggest that this diagnostic revolution has not yet been widely realised in SSA. A contributing factor may be that 23% of pregnant women still are not attended by a skilled healthcare worker even once during pregnancy, according to the 2010 WHO statistics.²⁰ This may account for the large proportion of patients presenting late and in extremis in our sample, which is consistent with the pattern of EP in SSA.² However, in Ghana, Obed showed that reliance on US as a diagnostic tool increased the diagnosis of unruptured EPs from a range of 0.3–1.1% in 1986–1989 to 8.5% in 1990.¹⁶ In Gabon, Picaud showed that diagnosis of unruptured EP increased from 17% to 50% from 1984–1987 with the use of US.²¹ Based on these studies, it appears that there are gains to be made from both the public health and clinical medicine sides.

The public health sector has targeted reduction in maternal mortality as one of the United Nations Millennium Development Goals for 2015. A component of this goal is improved antenatal care, which has already seen an increase from 69% in 1990 to 77% in 2010.³ Continued progress towards this goal should help to improve the opportunity for early diagnosis of pregnancy complications, for which US has been shown to be effective.^{1,2,4–6,22,23}

Our analysis shows an overall low rate (12.6%) of US utilisation in the work-up of EP when US was available, though one site used US as much as 80% of the time. This heterogeneity suggests that there is a wide variation in the application of US in workup of EP. The literature from Nigeria, South Africa, Kenya, and Botswana from 1974–2012 looked at viability of US programs regarding cost, training, and diagnostic test performance in low-resource settings with favourable results.^{24–33} Snyman’s review article, “Ultrasound in early pregnancy failure” concludes that US has replaced laparoscopy as the gold standard in the diagnosis of EP,³⁴ and Nkyekyer comments in a 2006 editorial titled, “Ectopic Pregnancy in Ghana- Time for A Change”, that “it is impera-

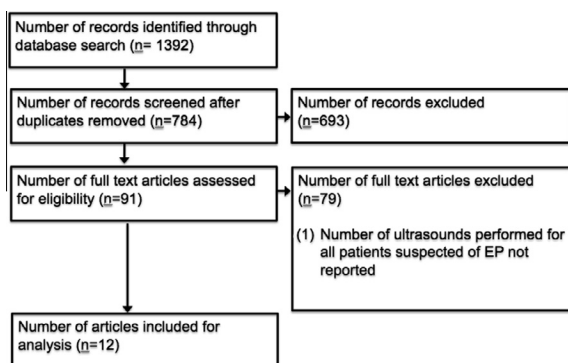


Figure 1. Results of the search strategy.

Table 1 Demographics of patients diagnosed with ectopic pregnancy.

Characteristic	<i>n</i>	No. of articles	Variable	<i>N</i>	(%)		
Age	1045	4	< 20 yo	39	(3.7)		
			20–34 yo	868	(83.1)		
			> 34 yo	130	(12.4)		
Parity	3393	7	Mean, in years	25.6			
			2420	6	P0	547	(22.6)
					$P \geq 1$	1873	(77.4)
Marital status	1678	2	Mean parity		(0.9)		
			504	3	Single	197	(39.0)
					Married	295	(58.5)
Unknown	12	(2.4)					
Education	2379	6	< Secondary	1738	(73.0)		
			> Secondary	624	(26.2)		
			Unknown	16	(0.7)		
Residence	470	3	Rural	194	(41.3)		
			Urban	238	(50.6)		
			Both	38	(8.1)		
History of abdominal or pelvic surgery	1539	3	Yes	67	(4.4)		
			No	1472	(95.6)		
History of previous ectopic pregnancy	3555	6	Yes	242	(6.8)		
			No	3313	(93.2)		
History of STI or PID	1843	4	Yes	154	(8.4)		
			No	1663	(90.2)		
			Not reported	26	(1.4)		

12 articles total. *n* = 6055.

Table 2 Summary of included articles.

Reference	Years	Hospital/Location	EP/Deliveries	US	B-HCG	Prior healthcare visit	Not aware	Ruptured	Shock	Mortality
Ali	2008–11	Maternity/Sudan	199/9578	118	11	52	183	186	98	1
Amoko	1992–93	Government/South Africa	148/13,000	74	136	–	–	106	92	3
Baffoe	1991–93	Teaching/Ghana	1255/31,788	163	–	87	–	1232	453	35
Dafallah	1997–99	Teaching/Sudan	88/16,221	71	–	–	–	80	16	3
Ikeme	1997–03	Teaching/Nigeria	136/6003	27	–	–	–	130	106	4
Kasule	1981–84	Teaching/Zimbabwe	441/162,964	23	–	–	–	321	233	1
Leke	2000	Population based/Cameroon	320/40,100	125	–	198	–	298	–	3
Obed	2000–03	Teaching/Ghana	1492/45,354	105	65/1411 ^a	473	1003/1411 ^a	1411	–	2
Obed	1986–90	Teaching/Ghana	1617/39,494	28/364 ^a	10/364 ^a	–	–	1578	–	2/364 ^a
Onah	2003–04	Teaching/Nigeria	19/–	19	19	–	–	15	15	–
Singh	2005–06	Teaching/South Africa	120/–	26	–	–	–	–	14	1
Thonneau	1995–99	Teaching/Guinea	220/–	10	7	–	–	200	–	0
Totals			(6055) ^b							
	N		5781	761	322	810	1186	5561	1031	55
	Patients		347,114	6055	3697	3253	1610	6027	2406	4783
	(%)		(1.7)	(12.6)	(8.7)	(25.0)	(73.7)	(92.3)	(42.9)	(1.1)

^a Study only reported on portion of total patients.

^b Total ectopic pregnancies reported in the 12 studies; 3 studies did not report the number of deliveries. The 5781 EP patients in the 9 in which deliveries were reported were used in the calculation of the EP rate.

tive that... ultrasound facilities be made available in poly clinics, and district and regional hospitals, with qualified personnel”³⁵

While widespread US referral facilities may not be feasible given the resources needed for facilities, US technologists to perform the scans, and radiologists to interpret the scans, bedside US performed by emergency physicians has been shown to exhibit excellent test characteristics for ruling out

EP in the United States. With dedicated emergency care training programs emerging across SSA, there is an opportunity to integrate training in bedside US in the work-up of suspected EP as a means to close the gap. In fact, the African Federation for Emergency Medicine consensus conference in 2011 advocated for this type of acute care safety net to address the Millennium Development Goal of reduction in maternal mortality.³⁶

Conclusion

The availability of US for the diagnosis of EP in SSA remains unclear. However, even among those sites reporting US availability, we found a wide variation in its utilisation in the diagnostic work-up of EP. Studies have shown that the addition of US alone can facilitate increased early EP diagnosis in SSA.^{16,21} Targeted public health interventions aimed at increasing maternal and provider awareness may also create a greater opportunity for earlier diagnosis of EP. Developing emergency care training programs in the region are poised to fill this clinical gap, much as they did in the United States and the United Kingdom. Together these interventions may lead to reduction in early pregnancy-related mortality similar to that observed in developed countries over the past 30 years.

Contributions

AHF was the primary investigator and author. SK was the second article reviewer and provided manuscript proof-reading and editing. GYW created the search strategy in consultation with AHF and provided edits on the methods section. JCS provided mentoring and oversight which included research design, analysis of results and manuscript edits. TR was the 3rd article reviewer and provided mentoring and oversight which included research design and manuscript edits.

Conflict of interest

The authors declare no conflict of interest.

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