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ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY OF ULTRASOUND IN EARLY DETECTION OF MOLAR PREGNANCY

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ABSTRACT

OBJECTIVE: To determine the diagnostic accuracy of ultrasound in detection of molar pregnancy taking histopathological findings as a gold standard.

METHODS: This study was conducted in Khyber Teaching Hospital, Peshawar, Pakistan. All pregnant females of 15-45 years' age; with clinical, biochemical suspicion and definite diagnosis of molar pregnancy were included in our study. Patients already diagnosed on histopathology as hydatidiform mole, missed miscarriage and invasive mole were excluded from the study. Informed consent, brief history, baseline investigations, serum beta human chorionic gonadotropin levels were obtained. Suspected cases of hydatidiform mole (n=212) on Transabdominal ultrasound scans were referred to gynecologist for histopathological diagnosis and management. Histopathology of samples were compared to ultrasound report. Data was collected was analyzed by SPSS v.23.0.

RESULTS: Mean age of patients was 29.04±8.23 years. Molar pregnancies were reported in 119 (56.13%) and 124 (58.49%) cases through ultrasound and histopathology respectively. Ultrasound findings suggestive of complete molar pregnancy in 79 (37.2%) cases, as compared to 85 (40.09%) cases by histopathology. Majority (n=35; 58.3%) of the molar pregnancy were found in patients having 31-40 years of age. Ultrasound and histopathology showed agreement in diagnosis of molar pregnancy in 103/156 (66%) cases and non-molar pregnancy in 40/56 (71.4%) cases. Sensitivity, specificity, positive predictive value, negative predictive value and overall diagnostic accuracy of ultrasound in diagnosis of molar pregnancy were 66.03%, 71.43%, 86.55% 43.01% and 67.45% respectively.

CONCLUSION: Overall diagnostic accuracy of ultrasound in diagnosis of molar pregnancy is 67.45% and may be used in early detection of molar pregnancy.

KEYWORDS: Molar Pregnancy (MeSH); Hydatidiform Mole (MeSH); Hydatidiform Mole, Complete (MeSH); Hydatidiform Mole, Partial (MeSH); Diagnostic accuracy (Non-MeSH); Diagnosis (MeSH); Ultrasound (MeSH); Diagnostic Imaging (MeSH).

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INTRODUCTION

Molar pregnancy is a pre-cancerous form of gestational trophoblastic disease which includes complete hydatidiform mole (CHM), partial hydatidiform mole (PHM), and the malignant forms. Malignant forms are invasive mole, choriocarcinoma and the placental trophoblastic tumor. CHM is the most common form of gestational trophoblastic disease.[1] Risk factors include extremes of maternal age, multiple births and previous history of molar pregnancy.[1,2]

International literature reported a variable data as Indonesia having 12/1000 cases of molar pregnancy. Overall incidence in Asia is 1 in 80 pregnancies as compared to the privileged countries.[3] In our country the incidence is recorded to be 28 per 1000 live births, in which 70% is found to be CHM and the remaining cases are formed by partial mole.[4]

Clinical presentation is abnormal bleeding in early pregnancy which is very difficult to differentiate from abortions due to other causes.[5] Ultrasound plays an important role as first line investigation along with serial beta human chorionic gonadotropin (hCG) monitoring.[6] The ultrasound diagnosis of a partial molar pregnancy is more complex; the finding of multiple soft markers, including both cystic spaces in the placenta and a ratio of transverse to anteroposterior dimension of the gestation sac of greater than 1.5, is required for the reliable diagnosis of a partial molar pregnancy.[7,8]

Fowler, et al., shows in his study that the sensitivity of ultrasound in detection of hydatidiform mole of any type is 44% and specificity is 74%.[9] Histological evaluation for the diagnosis of a complete mole is found sensitive in 91%, and 55% in partial mole and is found to be the gold standard.[8] A further study suggested a 56% detection rate for ultrasound examination.[10]

The patients after diagnosis of molar pregnancies are initially treated with evacuation and curettage but 10-20% of women with CHM develop persistent gestational trophoblastic disease. Persistent gestational trophoblastic disease incidence is 0.5-11% as cited by Lazarus, et al.[11]

Earliest detection of molar pregnancy is important for the expecting mother to prevent development of fatal complications, preserve fertility by reducing risk of hysterectomy and ensure prompt treatment. In undiagnosed cases even the benign forms have been shown to undergo invasive changes leading to lung metastasis. The majority of histologically proven complete moles are associated with an ultrasound diagnosis of delayed miscarriage or anembryonic pregnancy.

The whole management changes from a simple evacuation & curettage to serial chemotherapy sessions. There is an increasing demand from women for conservative or medical management of missed miscarriages where histopathological examination is not

TABLE I: AGE DISTRIBUTION (IN YEARS) OF THE STUDY SUBJECTS

Age Range (years)	Frequency (n=212)	Percentages
< 20	36	17%
20-30	91	42.9%
>30-40	60	28.3%
>41	25	11.8%

TABLE II: AGE WISE DISTRIBUTION OF THE STUDY SUBJECTS ON THE BASIS OF ULTRASOUND

Age (Years)	ULTRASOUND		TOTAL	P VALUE
	Molar pregnancy	No molar pregnancy		
<20	19 (52.8%)	17 (47.2%)	36	0.773
20-30	53 (58.2%)	38 (41.8%)	91	
>30-40	35 (58.3%)	25 (41.7%)	60	
>40	12 (48%)	13 (52%)	25	
Total	119 (56.1%)	93 (43.9%)	212	

TABLE III: ACCURACY OF ULTRASOUND IN DIAGNOSIS OF MOLAR PREGNANCY (N=212)

Variables		Frequency	Percentage
Ultrasound	Complete molar pregnancy	79	37.2
Histopathology	Partial molar pregnancy	40	18.86
	No molar pregnancy	93	43.86
	Complete molar pregnancy	85	40.09
	Partial molar pregnancy	39	18.39
	No molar pregnancy	88	41.5

TABLE IV: COMPARISON OF ULTRASOUND FINDINGS WITH HISTOPATHOLOGY IN DIAGNOSIS OF MOLAR PREGNANCY

Variables		Histopathology		Total
		Molar Pregnancy	No Molar Pregnancy	
Ultrasound	Molar Pregnancy	103 (66%)	16 (28.6%)	119
	No Molar Pregnancy	53 (34%)	40 (71.4%)	93
Total		156	56	212

available and the use of simple screening and follow-up techniques may reduce the number of cases that go unrecognized. Also the data regarding sensitivity, specificity in the literature is significantly variable. Ultrasound is easily accessible and cost effective. Histopathology is an expensive procedure, time consuming and costs the patient the unnecessary burden. The role of uterine artery resistive index on Doppler can still be studied in future cases. We planned this study to determine the diagnostic accuracy of ultrasound in detection of molar pregnancy taking histopathological findings as a gold standard in terms of establishing the proportion of patients who were truly diagnosed on ultrasound and also later on proved by histopathology.

METHODS

This validation study was conducted at department of Radiology and department of Gynecology/obstetrics, Khyber Teaching Hospital, Peshawar, Pakistan from November 2015 to May 2016. A sample of 212 patients was enrolled in the study using non-probability consecutive sampling. Sample size was calculated as 212, based on the prevalence of CHM 70%, margin of error 8% and 95% confidence interval.

All pregnant females of 15-45 years' age; with clinical, biochemical suspicion and definite diagnosis of molar pregnancy i.e. abnormal recurrent bleeding and/or exacerbated symptoms of pregnancy like repeated vomiting and/or large for dates on fundal height and/or abnormally raised beta hCG > 100,000 IU/L were included in our study. The criteria for ultrasound diagnosis was the presence of molar tissue there. An ultrasound scan shows a honeycomb structure made up of numerous vesicles. Bleeding into the uterus generates the snowfall-like aspect of the cysts as they expand. Massive cysts on the ovaries are relatively uncommon. While patients already diagnosed on histopathology as hydatidiform mole, missed miscarriage and invasive mole were excluded.

The study was commenced after approval from hospital's ethical and research board. Patients were either referred from in-patient or outpatient Gynecology Department of Khyber Teaching Hospital, Peshawar, Pakistan and were explained about the aim of procedure, use of data and publication of the study. Informed consent, brief history, baseline Investigations and the pregnancy test, serum beta hCG levels were obtained. Transabdominal ultrasound scans on full bladder were performed on Siemens, curved transducer. Patients with suspected hydatidiform mole were referred to gynecologist for the treatment and taking samples for histopathology and were sent to hospital laboratory for evaluation. Results were compared to ultrasound report.

The exclusion criteria were strictly followed to control confounders and exclude bias in study. All the results were followed by the researcher. All the above mentioned information was recorded in a pre-designed formula. Statistical Package for the Social Sciences (SPSS v.23.0) was used to analyze the data, wherein descriptive statistics were applied for both categorical and numerical variables. Post-stratification inferential statistics were applied for significance and validation, p-value ≤0.05 were taken as significant

RESULTS

A total of 212 patients were included in this study with clinical or biochemical suspicion of molar pregnancy. Mean age of the study subjects was 29.04±8.23 years. Majority (n=91; 42.9%) of patients were ranging in age from 20-30 years (Table I).

Age wise distribution of ultrasound results shows that majority (n=35; 58.3%) of the molar pregnancy were found in patients having 31-40 years of age (Table II). Ultrasound findings suggestive of complete molar pregnancy in 79 (37.2%) cases, as compared to 85 (40.09%) cases of complete molar pregnancy by histopathology. No molar pregnancy was reported in 93 (43.86%) through ultrasound and 88 (41.5%) cases by histopathology (Table III).

Comparison of ultrasound and histopathology showed agreement in diagnosis of molar pregnancy in 103 cases and non-molar pregnancy in 40 cases (Table IV). The sensitivity and specificity of ultrasound in diagnosis of molar pregnancy are 66.03% and 71.43% respectively while it has positive predictive value of 86.55% and negative predictive value of 43.01%. Overall the diagnostic accuracy of Ultrasound in diagnosis of molar pregnancy is 67.45%.

DISCUSSION

In this analysis, pre-operative ultrasound revealed more than fifty percent of complete and partial molar pregnancies, as compared to previously reported data. Prior to surgery, PHM were discovered at a significantly lower rate than CHM, according to a review of our data (Table III). Our population had slightly higher levels of particulate matter (PHM) than those found in earlier research, resulting in higher detection rates.

Non-surgical miscarriage treatments may be gaining popularity, but our findings over the past decade have been very constant. In 20% of cases, non-surgical therapy is beneficial; nevertheless, tissue from these miscarriages is rarely collected for histological research. Consequently, patients with PHM who were not surgically treated may have gone untreated. Because CHM increases dramatically with age,[9] it is probable that our EPU sample is older than previously investigated groups, but data for comparison are unavailable.

As transvaginal ultrasonography is increasingly utilized to detect early pregnancies, the frequency of molar pregnancies suspected prior to surgery has risen.[12-14] Even while computerized technologies may account for a portion of the growth in preoperative ultrasonography research in the United Kingdom, it is possible that previous studies employing paper-based clinical notes and outcomes were less accurate. The histological confirmation of a positive ultrasound diagnostic enabled us to discover and follow fetuses that appeared nonviable on ultrasound, as well as to assess the significance of a positive scan.[9]

Sonographers and clinicians should warn patients of the likelihood of molar pregnancy before choosing a miscarriage treatment.[15] Prior to this point, the majority of research on the diagnostic sensitivity of molar pregnancy concentrated on cases that were identified histologically. It would be fascinating to investigate whether or not our findings can be repeated across diverse clinical circumstances, individuals, and levels of supervision. To analyze the improvements in ultrasonographic molar pregnancy detection, the diagnostic process has not been evaluated for accuracy or consistency.[16]

A retrospective review of ultrasound scans (USS) of previously confirmed moles found that PHM were more likely to exhibit embryonic and extraembryonic characteristics that were easily discernible, as well as greater vascularity and less cystic placental tissue with no sac. hCG did not appear to be able to discern between the two based on their examination. Johns, et al.[12] found that ultrasonography is superior at detecting high levels of hCG in the CHM than in the PHM. Due to the huge amount of chorionic tissue and lack of typical gestational sac architecture, USS could have discovered some cases of CHM prior to surgery if it had been conducted by more proficient sonographers. Therefore, distinguishing PHM from a simple first-trimester loss may be challenging.

In response to early embryonic apoptosis, to evaluate diagnostic criteria, an organized investigation employing specific evaluation criteria must be done. After surgical treatment of miscarriage, there is a controversy in the United Kingdom regarding the expense and efficacy of tissue histological analysis.[17] When a simple pregnancy test after a miscarriage can identify the few instances of persistent GTD, a PHM diagnosis is pointless. In the United Kingdom, there is no longer a six-month waiting time for conceiving again after a pregnancy loss; as a result, histology is no longer required and the risk of developing CHM is less than 1%.[18] Despite the extremely low risk of recurrence, women's anxiety about future pregnancies may be exacerbated by their knowledge of underlying PHM. However, there is scant evidence to support the notion that the diagnosis will reduce anxiety

LIMITATIONS OF THE STUDY

Our investigation was hindered by the complexity of analysing historical data. We were convinced that the ultrasound data accurately diagnosed all molar pregnancy cases. Due to the fact that our gynecologist sonographers discovered an underlying molar pregnancy and desired histological analysis of the remnants, it is conceivable that they recommended surgical treatment for a miscarriage. Patients with negative CT scans and no histology tissue for further examination are presumed to be free of GTD. Unfortunately, it is probable that the molar status of some pregnancies that were expected to result in miscarriage was never identified. The real rate of false negatives cannot be determined without a comprehensive histological analysis of the entire specimen.

CONCLUSION

The overall diagnostic accuracy of Ultrasound in diagnosis of molar pregnancy is 67.45%. The ultrasound examination is more reliable in the diagnosis of complete hydatidiform mole when compared to partial hydatidiform mole. Detecting molar pregnancy with ultrasonography remains a diagnostic challenge, particularly for PM patients. Despite the fact that the diagnostic criteria for ultrasound have evolved over time, our findings indicate that they remain ambiguous and vigilance is required to look for all the ultrasound imaging signs of molar pregnancy.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

KB: Concept, acquisition, analysis and interpretation of data, drafting the manuscript, critical review, approval of the final version to be published.

HG & Mu: Acquisition of data, drafting the manuscript, approval of the final version to be published.

KN: Concept and study design, drafting the manuscript, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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CONFLICT OF INTEREST

Authors declared no conflict of interest

DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request