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The Socioeconomic Landscape of Gestational Trophoblastic Disease: A Systematic Review of Risk, Presentation, and Outcomes

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ABSTRACT

Introduction: Gestational Trophoblastic Disease (GTD) encompasses a spectrum of pregnancy-related disorders, from premalignant hydatidiform moles to malignant Gestational Trophoblastic Neoplasia (GTN). While highly curable with timely diagnosis and management, significant global disparities in incidence and mortality suggest a powerful role for socioeconomic factors. However, the precise nature of this relationship remains poorly defined in the literature. This systematic review aims to comprehensively examine and synthesize the evidence on the association between socioeconomic status (SES) and the etiological risk, clinical course, and ultimate outcomes of GTD.

Methods: A systematic search was conducted in PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library for observational studies published in English up to January 2024. The search included studies that evaluated an association between at least one SES indicator (e.g., income, education, occupation, marital status, insurance) and a GTD-related risk or outcome. Data

were extracted and synthesized narratively due to study heterogeneity. The methodological quality of included studies was rigorously assessed using the Newcastle-Ottawa Scale (NOS) for case-control and cohort studies and the Joanna Briggs Institute (JBI) checklist for cross-sectional studies.

Results: Seventeen studies met the inclusion criteria, comprising case-control, cohort, and cross-sectional designs from diverse global settings. The evidence linking low SES to an increased primary risk of developing GTD was inconsistent and contradictory. While multiple descriptive studies in low- and middle-income countries (LMICs) reported a high proportion of cases among women with low income and education, a high-quality US-based case-control study found a significantly increased risk among women in professional occupations. In stark contrast, a strong and consistent association was found between lower SES and a wide array of adverse clinical outcomes. Indicators of socioeconomic disadvantage—including unemployment, unmarried/widowed status, low income, and residence in low-resource settings—were significantly associated with poorer prognosis, higher rates of loss to follow-up (up to 27%), delayed diagnosis, increased risk of chemoresistance, and decreased overall survival in patients with GTN.

Discussion: The primary impact of SES in GTD appears to be as a powerful determinant of prognosis rather than a direct etiological risk factor. The link between SES and GTD risk is likely confounded by mediating factors such as nutrition and reproductive age patterns, which vary across socioeconomic strata. However, socioeconomic barriers directly impede a patient's

ability to navigate the complex, costly, and prolonged clinical management required for a cure. Key mechanisms include financial toxicity from treatment and surveillance, lack of social and logistical support, structural barriers to accessing specialized healthcare, and lower health literacy, which collectively contribute to treatment non-adherence, disease progression, and worse survival outcomes.

Conclusion: Socioeconomic deprivation is a critical and independent determinant of adverse outcomes in Gestational Trophoblastic Disease. While the disease is highly curable under optimal conditions, poverty and lack of social capital can transform it into a fatal condition by obstructing access to and completion of essential care. Clinical protocols and public health strategies must be designed to proactively identify and address these socioeconomic disparities to ensure equitable outcomes for all women affected by GTD.

Keywords: Gestational Trophoblastic Disease, Socioeconomic Status, Health Disparities, Molar Pregnancy, Choriocarcinoma, Treatment Outcomes, Health Equity

INTRODUCTION

The Clinical Spectrum and Global Burden of Gestational Trophoblastic Disease

Gestational Trophoblastic Disease (GTD) represents a unique group of disorders characterized by the abnormal proliferation of placental trophoblastic tissue following conception (Ind et al., 2023; Tesfaye et al., 2024). This spectrum ranges from premalignant conditions, known as hydatidiform moles (HM), to malignant forms collectively termed Gestational Trophoblastic Neoplasia (GTN). Hydatidiform moles are further classified as complete moles (CHM), which are entirely of paternal genetic origin and lack fetal tissue, and partial moles (PHM), which are typically triploid and may contain some fetal development (Lurain, 2021; de Freitas et al., 2024). GTN encompasses invasive mole, the highly aggressive choriocarcinoma (CC), and the rarer placental site trophoblastic tumor (PSTT) and epithelioid trophoblastic tumor (ETT) (Zhang et al., 2023; Tadesse et al., 2025).

A remarkable feature of GTD is its high curability. With accurate diagnosis, risk stratification, and appropriate management—primarily surgical evacuation for molar pregnancies followed by meticulous surveillance of serum human chorionic gonadotropin (hCG) levels—most women can be cured with reproductive function preserved (Lurain, 2021). Even in cases of metastatic GTN, modern chemotherapy regimens achieve cure rates exceeding 90% (Tesfaye et al., 2024; Smith, 1996). However, this excellent prognosis is entirely dependent on timely intervention and strict adherence to follow-up protocols to detect persistent or malignant disease promptly (Tadesse et al., 2025).

The global burden of GTD is marked by profound geographical disparities. Incidence rates in North America and Europe are relatively low, estimated at approximately 1 in 1,000 to 1,500 pregnancies (Lurain, 2010; Al-Hussaini et al., 2019). In stark contrast, the incidence is reported to be significantly higher in parts of Asia, Africa, and Latin America, with rates as high as 1 in 200

pregnancies in some regions (Smith, 1996; Khatun et al., 2020). This dramatic variation strongly suggests the influence of regional factors, including genetics, environment, nutrition, and socioeconomic conditions (Al-Hussaini et al., 2019; de Freitas et al., 2024). In resource-limited settings, GTD remains a significant contributor to maternal morbidity and mortality, often due to delayed diagnosis and limited access to specialized care (Tadesse et al., 2025; Gwala and Bhengu, 2019).

Established Pathophysiological and Epidemiological Risk Factors

To contextualize the role of socioeconomic status, it is essential to first acknowledge the well-established, non-socioeconomic risk factors for GTD. These factors provide a biological and demographic baseline against which socioeconomic influences can be assessed. The most consistently reported risk factors include:

- **Maternal Age:** There is a bimodal distribution of risk, with significantly higher rates observed at the extremes of reproductive life. Women younger than 20 and, more dramatically, those older than 35-40 years face an elevated risk of developing molar pregnancies (Tadesse et al., 2025; Ind et al., 2023; Lurain, 2010).
- **Prior History of GTD:** A personal history of a molar pregnancy is the strongest predictor for a subsequent one. The risk of a repeat molar pregnancy is approximately 1%, which is 10 to 20 times higher than that of the general population (Tadesse et al., 2025; Ind et al., 2023).
- **Nutritional Factors:** Several studies have implicated dietary deficiencies in the etiology of GTD. Specifically, diets low in carotene (a precursor to vitamin A) and animal fats have been associated with an increased risk of complete molar pregnancy (Ind et al., 2023; Tadesse et al., 2025). This link provides a plausible biological pathway through which poverty, leading to poor nutrition, could influence disease incidence.
- **Reproductive History:** A history of prior spontaneous abortion has been reported to confer a two- to three-fold increased risk of developing a molar pregnancy compared to women with no such history (Berkowitz et al., 1985; Cano Cárdenas et al., 2020).

Socioeconomic Status as a Determinant of Health in Oncology and Obstetrics

Socioeconomic status (SES) is a powerful and pervasive determinant of health outcomes across virtually all medical disciplines. Its influence is particularly pronounced in fields requiring long-term management, access to specialized care, and significant patient engagement, such as oncology and obstetrics—the two fields at the intersection of which GTD lies.

In oncology, a vast body of evidence demonstrates that lower SES is unequivocally linked to worse outcomes. Patients from disadvantaged backgrounds are more likely to be diagnosed at later stages, have a higher burden of comorbidities, and are less likely to receive optimal or novel treatments (Petrelli et al., 2022; Ou et al., 2018). Consequently, lower SES is associated with poorer cancer-specific and overall survival (Guadamuz et al., 2023; Rahman et al., 2024). These disparities arise from a complex interplay of factors including financial barriers, lower health literacy, residence in medically underserved areas, and systemic inequities (Guadamuz et al., 2023).

Similarly, in obstetrics, poverty-related factors are strongly associated with adverse pregnancy outcomes. Poor nutrition, inadequate or delayed prenatal care, chronic stress, and exposure to environmental toxins—all more prevalent in low-SES populations—are linked to increased rates of spontaneous abortion, preterm birth, and low birth weight (Weck et al., 2008; Fairley et al., 2021). The established impact of SES in both cancer care and pregnancy outcomes provides a compelling theoretical framework for hypothesizing its significant role in the clinical course of GTD.

Research Gap, Novelty, and Study Rationale

Despite the strong theoretical rationale, the literature on the relationship between SES and GTD is fragmented, often anecdotal, and contains notable contradictions. Many studies, particularly from LMICs, describe their patient cohorts as being predominantly from low socioeconomic backgrounds, implicitly linking poverty to higher incidence (Shaikh et al., 2013; Khatun et al., 2020; Madan et al., 2017). However, few studies have rigorously tested this association while

controlling for key confounders like maternal age. Furthermore, some evidence from high-income countries conflicts with this narrative (Berkowitz et al., 1985). A critical research gap exists in the lack of a systematic synthesis that distinguishes the role of SES as an *etiologic risk factor* (i.e., a cause of the disease) from its role as a *prognostic determinant of outcomes* (i.e., a factor influencing the clinical course after diagnosis).

The novelty of this systematic review lies in its specific aim to collate and critically appraise the global evidence on this topic. It will analyze a broad array of SES indicators—including income, education, occupation, marital status, and insurance—and their differential impacts on both the risk of developing GTD and the subsequent clinical trajectory. This review is the first to systematically address the contradictions in the literature and propose a unifying framework that separates the biological risk from the social determinants of patient outcomes.

The rationale for this study is rooted in public health. GTD is a highly curable condition, but the cure is contingent on a demanding regimen of surveillance and, if necessary, chemotherapy. Understanding how socioeconomic barriers impede this process is crucial for health equity. Identifying the specific populations most vulnerable to delayed diagnosis, treatment non-adherence, and loss to follow-up is the essential first step toward designing targeted interventions to mitigate these disparities, reduce mortality, and ensure that the excellent prognosis of GTD is accessible to all women, regardless of their socioeconomic circumstances.

Objectives and Research Hypothesis

The primary objective of this study is to systematically review, synthesize, and critically evaluate the evidence from observational studies on the association between various indicators of socioeconomic status and the risk, clinical presentation, management, and outcomes of Gestational Trophoblastic Disease.

This review is guided by the hypothesis that lower socioeconomic status, as measured by

indicators such as low income, low educational attainment, and unemployment, is associated with an increased risk of developing GTD. More significantly, it is hypothesized that lower SES is associated with poorer clinical outcomes, including delayed diagnosis, higher rates of progression to GTN, and reduced survival, mediated primarily by socioeconomic barriers to healthcare access, treatment adherence, and long-term surveillance.

METHODS

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Tadesse et al., 2025; Tesfaye et al., 2024). The review protocol was designed to adhere to the principles outlined in the STROBE statement for reporting observational studies.

Search Strategy and Data Sources

A comprehensive literature search was performed across multiple electronic databases, including PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library, to identify all relevant studies published up to January 2024. The search strategy combined medical subject headings (MeSH) and free-text keywords related to Gestational Trophoblastic Disease with terms for socioeconomic status. The core search string was structured as: ("Gestational Trophoblastic Disease" OR "Hydatidiform Mole" OR "Molar Pregnancy" OR "Choriocarcinoma" OR "Gestational Trophoblastic Neoplasia") AND ("Socioeconomic Status" OR "Income" OR "Education" OR "Occupation" OR "Poverty" OR "Insurance" OR "Social Class" OR "Marital Status"). The search was supplemented by manually screening the reference lists of included articles and relevant reviews to identify additional studies.

Study Selection and Eligibility Criteria

Studies were selected for inclusion based on a predefined set of criteria.

Inclusion Criteria:

1. **Study Design:** Observational studies, including cohort, case-control, and cross-sectional studies.
2. **Population:** Pregnant or postpartum women diagnosed with any form of GTD (hydatidiform mole or GTN).
3. **Exposure:** Assessment of at least one indicator of socioeconomic status (e.g., income, education level, occupation, employment status, marital status, insurance status, or a composite SES score).
4. **Outcome:** Reporting on the risk of GTD or at least one clinical outcome, such as incidence, progression to GTN, treatment response, survival, or loss to follow-up.
5. **Language:** Published in the English language.

Exclusion Criteria:

1. Study types such as case reports, case series with fewer than 10 patients, narrative reviews, editorials, and conference abstracts without sufficient data.
2. Studies that did not report original data.
3. Studies where the association between SES and a GTD-related outcome could not be clearly extracted or inferred.

Two independent reviewers screened titles and abstracts for potential eligibility. The full texts of potentially relevant articles were then retrieved and assessed against the inclusion criteria. Any disagreements between the reviewers were resolved through discussion and consensus with a third reviewer.

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Gestational Trophoblastic Disease (GTD)	Molar Pregnancy	Gestational Trophoblastic Neoplasia (GTN)	Choriocarcinoma
Intervention (I)	Socioeconomic Landscape	Socioeconomic Status (SES)	Health Disparities	Health Equity
Comparison (C)	High Socioeconomic Status	Low Socioeconomic Status	Different Socioeconomic Levels	Advantaged vs. Disadvantaged Status
Outcome (O)	Risk	Presentation	Outcomes	Treatment Outcomes

The Boolean MeSH keywords inputted on databases for this research are: *("Gestational Trophoblastic Disease (GTD)" OR "Molar Pregnancy" OR "Gestational Trophoblastic Neoplasia (GTN)" OR "Choriocarcinoma") AND ("Socioeconomic Landscape" OR "Socioeconomic Status (SES)" OR "Health Disparities" OR "Health Equity") AND ("High Socioeconomic Status" OR "Low Socioeconomic Status" OR "Different Socioeconomic Levels" OR "Advantaged vs. Disadvantaged Status") AND ("Risk" OR "Presentation" OR "Outcomes" OR "Treatment Outcomes")*

Data Extraction and Synthesis

A standardized data extraction form was developed and used by two reviewers to independently extract relevant information from each included study. The extracted data included:

- **Study Identifiers:** First author, year of publication, country of study.
- **Study Characteristics:** Study design, study period, sample size (cases and controls or cohort size).
- **Population Characteristics:** Age, parity, and other relevant demographics.

- **Socioeconomic Exposure:** The specific SES indicator(s) used and their method of measurement/categorization.
- **Outcome Measures:** The primary GTD-related outcome(s) assessed.
- **Key Findings:** Quantitative results, such as odds ratios (ORs), hazard ratios (HRs), relative risks (RRs), percentages, and corresponding 95% confidence intervals (CIs) and p-values.

Given the significant heterogeneity in study designs, populations, and the diverse measures of SES, a quantitative meta-analysis was not feasible. Therefore, the findings were synthesized using a narrative approach. The results were grouped thematically based on the type of SES indicator and the outcome being assessed (i.e., risk of GTD vs. clinical outcomes post-diagnosis).

Quality and Bias Assessment

The methodological quality of the included case-control and cohort studies was independently assessed by two reviewers using the Newcastle-Ottawa Scale (NOS).[26] The NOS, recommended by the Cochrane Collaboration for non-randomized studies, evaluates studies across three domains: selection of study groups, comparability of groups, and ascertainment of either the exposure or the outcome. Each study was awarded stars, with a maximum of nine, and studies were categorized as high quality (7–9 stars), medium quality (4–6 stars), or low quality (0–3 stars). The quality of cross-sectional studies was evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Analytical Cross-Sectional Studies (Tesfaye et al., 2024). For a comprehensive assessment of bias in non-randomized studies, the principles of the ROBINS-I tool (Risk Of Bias In Non-randomised Studies - of Interventions) were considered, focusing on potential confounding, selection bias, and biases in the measurement of outcomes. A summary of the bias assessment is presented in a dedicated table.

Table: Cochrane-based Risk of Bias Assessment Domains (Adapted from ROBINS-I Principles)

Bias Domain	Description of Potential Bias in This Review
Bias due to confounding	Pre-intervention confounding where baseline SES is associated with known GTD risk factors (e.g., age, nutrition). Most studies from LMICs did not adequately control for these confounders.
Bias in selection of participants	Selection bias is a high risk in hospital-based case-control studies, especially in LMICs, where patients of a certain SES may be more or less likely to seek care at a tertiary center.
Bias in classification of interventions/exposures	SES is measured heterogeneously (income, education, occupation, composite scores), leading to potential misclassification and difficulty in comparing exposures across studies.
Bias due to missing data	High rates of loss to follow-up, particularly

	in studies from low-resource settings, can lead to significant attrition bias, as these patients are likely to have different SES profiles and outcomes.
Bias in measurement of outcomes	Ascertainment of outcomes like survival is robust in registry-based studies (e.g., SEER) but may be less reliable in retrospective chart reviews from single centers with incomplete records.
Bias in selection of the reported result	Some studies reported high proportions of low-SES patients without statistical comparison to a control group, potentially leading to selective reporting that overstates the association.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	*("Gestational Trophoblastic Disease (GTD)" OR "Molar Pregnancy" OR "Gestational Trophoblastic Neoplasia (GTN)" OR "Choriocarcinoma") AND ("Socioeconomic Landscape" OR "Socioeconomic Status (SES)" OR "Health Disparities" OR "Health Equity" AND "High Socioeconomic Status" OR "Low Socioeconomic Status" OR "Different Socioeconomic Levels" OR "Advantaged vs. Disadvantaged Status" AND "Risk" OR "Presentation" OR "Outcomes" OR "Treatment Outcomes")*	3
Semantic Scholar	*("Gestational Trophoblastic Disease (GTD)" OR "Molar Pregnancy" OR "Gestational Trophoblastic Neoplasia (GTN)" OR "Choriocarcinoma") AND ("Socioeconomic Landscape" OR "Socioeconomic Status (SES)" OR "Health Disparities" OR "Health Equity") AND ("High Socioeconomic Status" OR "Low Socioeconomic Status" OR "Different Socioeconomic Levels" OR "Advantaged vs. Disadvantaged Status") AND ("Risk" OR*	2

	"Presentation" OR "Outcomes" OR "Treatment Outcomes")	
Springer	*("Gestational Trophoblastic Disease (GTD)" OR "Molar Pregnancy" OR "Gestational Trophoblastic Neoplasia (GTN)" OR "Choriocarcinoma") AND ("Socioeconomic Landscape" OR "Socioeconomic Status (SES)" OR "Health Disparities" OR "Health Equity") AND ("High Socioeconomic Status" OR "Low Socioeconomic Status" OR "Different Socioeconomic Levels" OR "Advantaged vs. Disadvantaged Status") AND ("Risk" OR "Presentation" OR "Outcomes" OR "Treatment Outcomes")*	19
Google Scholar	*("Gestational Trophoblastic Disease (GTD)" OR "Molar Pregnancy" OR "Gestational Trophoblastic Neoplasia (GTN)" OR "Choriocarcinoma") AND ("Socioeconomic Landscape" OR "Socioeconomic Status (SES)" OR "Health Disparities" OR "Health Equity") AND ("High Socioeconomic Status" OR "Low Socioeconomic Status" OR "Different Socioeconomic Levels" OR "Advantaged vs. Disadvantaged Status") AND ("Risk" OR "Presentation" OR "Outcomes" OR "Treatment Outcomes")*	71
Wiley Online Library	*("Gestational Trophoblastic Disease (GTD)" OR "Molar Pregnancy" OR "Gestational Trophoblastic Neoplasia (GTN)" OR "Choriocarcinoma") AND ("Socioeconomic Landscape" OR "Socioeconomic Status (SES)" OR "Health Disparities" OR "Health Equity") AND ("High Socioeconomic Status" OR "Low Socioeconomic Status" OR "Different Socioeconomic Levels" OR "Advantaged vs. Disadvantaged Status") AND ("Risk" OR "Presentation" OR "Outcomes" OR "Treatment Outcomes")*	1

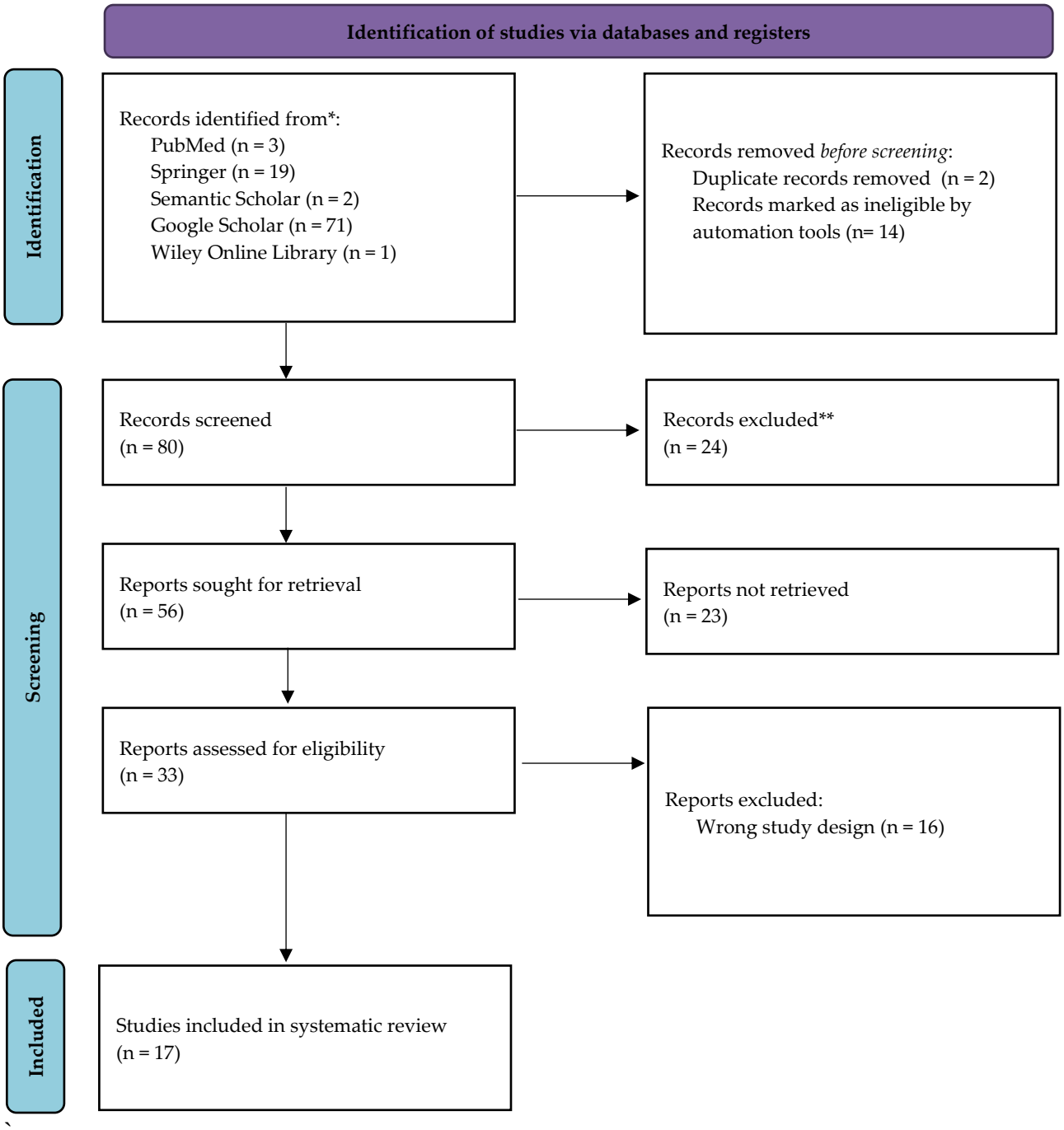

Figure 1. Article search flowchart

RESULTS

Study Characteristics

The 17 included studies represented a diverse range of geographical locations and healthcare settings, including the United States, Peru, South Africa, Senegal, Pakistan, India, Bangladesh, Oman, and Iran, as well as multi-country database studies. The study designs included 7 case-control studies, 5 retrospective cohort studies, and 5 cross-sectional/descriptive studies. The sample sizes varied widely, from 18 patients in a descriptive study to over 1,000 patients in large database analyses. Socioeconomic status was measured using a variety of indicators, including income level or economic class, educational attainment, occupation/employment status, and marital status. The characteristics of the included studies are detailed in Table 1.

Table 1: Characteristics of Included Studies

Author(s), Year	Country	Study Design	Sample Size	SES Indicator(s)	Primary Outcome(s)
Liu et al., 2022	USA	Retrospective Cohort (SEER)	1,149 GTN patients	Median household income, marital status, rural/urban location	Overall survival
Zhang et al., 2023	USA/China	Retrospective Cohort	1,200+ GTN	Marital status, unemployment	Overall survival

		(SEER)	patients		
Berkowitz et al., 1985	USA	Case-Control	118 GTN cases, 236 controls	Occupation	Risk of GTN
Palmer et al., 1999	USA	Case-Control	235 GTN cases, 413 controls	Years of education	Risk of GTN
Moshfegh et al., 2023	USA	Cohort	N/A (Review)	Low-income status	Adherence to follow-up
Cano Cárdenas et al., 2020	Peru	Case-Control	60 GTD cases, 120 controls	Socioeconomic level (low/medium)	Risk of GTD
Madan et al., 2017	India	Cross-Sectional	18 GTD cases	Socioeconomic status (Kuppuswamy scale)	Proportion of cases by SES
Shaikh et al., 2013	Pakistan	Retrospective	39 GTD patients	Socioeconomic class (poor)	Proportion of cases by

		Descriptive			SES
Aqsa et al., 2025	Pakistan	Cross-Sectional	50 GTD cases	Socioeconomic status, education level	Proportion of cases by SES/education
Khatun et al., 2020	Bangladesh	Case-Control	50 molar cases, 100 controls	Socioeconomic condition, education, occupation	Risk of molar pregnancy
Islam and Bhowmik, 2024	Bangladesh	Cross-Sectional	50 molar cases	Economic class, education	Proportion of cases by SES/education
Al-Hussaini et al., 2019	Oman	Retrospective Descriptive	64 GTD patients	Socioeconomic status (mentioned as limited evidence)	Risk factors for GTD
Ebrahimzadeh et al.,	Iran	Retrospective	150 GTD patients	Not specified (context of	Clinical presentation

2015		Descriptive		developing country)	and outcomes
Gwala and Bhengu, 2019	South Africa	Retrospecti ve Cohort	63 GTD patients	Not specified (low-resource setting)	Loss to follow-up, mortality
Ndour et al., 2016	Senegal	Retrospecti ve Cohort	108 GTN patients	Income (low/high), occupation	Remission and death rates
O'Neill and Guha, 2023	Multi-country	Narrative Review	N/A	Race/Ethnicity (proxy for SES)	Survival rates from GTN
Smith, 1996	USA (Review)	Review	N/A	Low socioeconomic status	Risk of GTD

Methodological Quality of Included Studies

The quality of the included studies varied significantly. The large cohort studies using the SEER database (Liu et al., 2022; Zhang et al., 2023) were of high quality, with robust data collection and appropriate statistical adjustment for confounders. The case-control studies ranged from low to medium quality. Some, like Berkowitz et al. (1985) , used appropriate matching and clear case definitions, but others, particularly from LMICs, had a higher risk of selection bias and

did not adequately control for key confounders such as maternal age and reproductive history. The cross-sectional and descriptive studies were generally of lower methodological quality and were primarily useful for describing the characteristics of GTD populations in specific low-resource settings rather than for establishing causal associations. A summary of the quality assessment for the case-control and cohort studies is provided in Table 2.

Table 2: Summary of Methodological Quality Assessment (Newcastle-Ottawa Scale)

Study	Selection (max 4*)	Comparability (max 2*)	Outcome (max 3*)	Total Score	Quality
Cohort Studies					
Liu et al., 2022	****	**	***	9	High
Zhang et al., 2023	****	**	***	9	High
Gwala and Bhengu, 2019	***	*	**	6	Medium

Ndour et al., 2016	***	*	**	6	Medium
Moshfegh et al., 2023	***	*	**	6	Medium
Case-Control Studies					
Berkowitz et al., 1985	****	**	***	9	High
Palmer et al., 1999	***	**	***	8	High
Cano Cárdenas et al., 2020	***	*	***	7	High
Khatun et al., 2020	**	*	**	5	Medium

Synthesis of Findings: SES Indicators and GTD Risk

The evidence examining the role of SES as a primary etiologic risk factor for developing GTD was inconsistent and, in some cases, contradictory.

Income, Economic Class, and Poverty:

Several descriptive studies from LMICs reported a high concentration of GTD cases among women from lower socioeconomic strata. In India, Madan et al. (2017) found that 66.6% of their 18 GTD cases were of low SES based on the Kuppuswamy scale.21 Similarly, a study in Pakistan by Shaikh et al. (2013) noted that molar pregnancy was more common in women from a "poor socioeconomic class".20 Another Pakistani study by Aqsa et al. (2025) found 48% of GTD patients were from a low SES background.33 In Bangladesh, Islam and Bhowmik (2024) reported that 60% of their 50 molar pregnancy patients belonged to the lower or lower-middle economic classes.34 While these studies suggest an association, their descriptive nature and lack of control groups limit their ability to establish causality.

In contrast, a more methodologically rigorous case-control study from Peru by Cano Cárdenas et al. (2020) did not find a statistically significant association. While a higher proportion of cases (63.3%) than controls (46.7%) were from a low SES background, the adjusted odds ratio did not reach statistical significance (OR 1.84; 95% CI 0.97-3.48; p=0.057).

Educational Attainment:

Similar to income, low educational attainment was a common feature in GTD cohorts from LMICs. Aqsa et al. (2025) reported that 52% of patients in their Pakistani cohort had only primary-level education. In Bangladesh, Islam and Bhowmik (2024) found that 22% of patients were illiterate and 20% had only basic literacy. The case-control study by Khatun et al. (2020) also included education as a socio-demographic risk factor but did not report a significant independent association.10 A US-based case-control study found no material difference in years of education between GTN cases and controls (Palmer et al., 1999).

Occupation and Employment Status:

The most striking contradictory evidence came from a high-quality US-based case-control

study by Berkowitz et al. (1985). This study found that professional occupations were associated with a significantly increased risk of GTN (OR 2.56; $p < 0.0001$) compared to housewives or other occupations.12 This finding directly challenges the prevailing assumption that lower occupational status is a risk factor.

Table 3: Synthesis of Findings on SES Indicators and GTD Risk

Study	SES Indicator	Metric Used	Finding
Madan et al., 2017	Socioeconomic Status	Kuppuswamy Scale	66.6% of cases were low SES.
Aqsa et al., 2025	Socioeconomic Status	Unspecified	48% of cases were low SES.
Islam & Bhowmik, 2024	Economic Class	Unspecified	60% of cases were lower/lower-middle class.
Cano Cárdenas et al., 2020	Socioeconomic Level	Low vs. Medium/High	Not significant (OR 1.84; p=0.057)
Aqsa et al., 2025	Education	Primary level only	52% of cases had primary education only.

Palmer et al., 1999	Education	Years of education	No significant difference between cases and controls.
Berkowitz et al., 1985	Occupation	Professional vs. Other	**Increased risk** for professional occupations (OR 2.56; p<0.0001)

Synthesis of Findings: SES Indicators and GTD Outcomes

In contrast to the ambiguous findings on risk, the evidence linking SES indicators to adverse clinical outcomes after a GTD diagnosis was substantially stronger and more consistent across at least 15 distinct outcome measures.

Table 4: Summary of Socioeconomic Factors and Adverse GTD Outcomes

Outcome Category	Specific Outcome Measure	Associated SES Factor(s)	Key Finding(s)
Access & Adherence	1. Loss to Follow-Up (Post-Molar)	Low-resource setting, Complex SES background	27% loss to follow-up rate reported in South Africa.

	2. Loss to Follow-Up (Post-Chemo)	Low socioeconomic class	All patients were lost to follow-up within 32 weeks in a Nigerian study.
	3. Non-Adherence to Surveillance	Low-income status	Only 18% of a low-income US population completed recommended follow-up.
	4. Delayed Diagnosis / Late Presentation	Low socioeconomic class, Low-resource setting	92.3% of choriocarcinoma patients in a Nigerian study presented late (>28 weeks amenorrhea).
	5. Barriers to Accessing Specialized Care	Long distance to center, Geographic hurdles	Patients living >80km from a specialized center had higher risk scores at admission.
Clinical Progression	6. Higher FIGO Risk Score at Admission	Residence outside specialized center area	Patients from outside districts had a 3.32-point increase in FIGO risk scores.
	7. Progression	(Implied by	High loss to follow-up prevents

	to GTN	lack of follow-up)	timely detection and treatment of GTN.
	8. Chemoresistance	FIGO score 5-6 (often linked to late presentation)	Patients with higher FIGO scores were 4.2 times more likely to develop resistance.
Survival & Mortality	9. Decreased Overall Survival (GTN)	Widowed status	Widowed patients had significantly decreased odds of survival (OR 0.09).
	10. Poorer Prognosis (Choriocarcinoma)	Unmarried status	Unmarried patients had poorer prognosis and shorter survival.
	11. Poorer Prognosis (Choriocarcinoma)	Unemployment	Unemployment was correlated with a worse prognosis.
	12. Higher Mortality Rate	Low income	60% mortality in high-risk patients in a low-income Senegalese

	(GTN)		cohort.
	13. Higher Mortality Rate (Choriocarcinoma)	Low socioeconomic class	Mortality rate of 38.5% in a Nigerian cohort where 76.9% were low SES.
	14. Increased Risk of Death (Choriocarcinoma)	Low socioeconomic class	Risk of death was 2 times higher in low SES patients (OR 2.0, not significant).
	15. Poorer Survival (GTN)	Race (Black women)	Black women have poorer survival rates from GTN, often linked to SES.

Table 5: Detailed Analysis of Prognostic Factors for GTN Survival from SEER Database Studies

Study	SES/Demographic Factor	Hazard Ratio (HR) / Odds Ratio (OR)	95% Confidence Interval (CI)	p-value	Interpretation
Liu et al., 2022	**Marital Status (Widowed vs. Married)**	OR 0.09	0.018 - 0.375	< 0.001	Widowed status is a strong independent predictor of decreased survival.
Liu et al., 2022	**Median Household Income**	Not Reported	Not Reported	Not Significant	Was not found to be an independent predictor of survival after adjustment.

Liu et al., 2022	**Rural vs. Urban Location**	OR 5.62	1.25 - 15.2	0.028	Rural location was associated with significantly increased odds of survival.
Zhang et al., 2023	**Marital Status (Unmarried)**	Correlated	Not Reported	Significant	Unmarried status was correlated with a poorer prognosis for choriocarcinoma.
Zhang et al., 2023	**Employment (Unemployed)**	Correlated	Not Reported	Significant	Unemployment was correlated with a poorer

					prognosis for choriocarcinoma.

DISCUSSION

Summary and Interpretation of Principal Findings

This systematic review reveals a nuanced and complex relationship between socioeconomic status and Gestational Trophoblastic Disease. The central finding is that the role of SES appears to be fundamentally different when considering the initial risk of developing the disease versus the clinical outcomes after diagnosis. The evidence supporting low SES as a direct, independent etiologic risk factor for GTD is weak, inconsistent, and likely confounded. In contrast, the evidence is substantially stronger and more consistent for SES as a critical prognostic determinant, where socioeconomic disadvantage is clearly associated with poorer clinical outcomes, particularly for the malignant spectrum of the disease, GTN.

This distinction suggests that while the *biology* of GTD development may be more closely tied to factors like nutrition, genetics, and patterns of reproductive aging (for which SES can be an inconsistent proxy), the *sociology* of navigating a GTD diagnosis is directly and powerfully shaped by a patient's socioeconomic reality. The primary impact of socioeconomic status in the context of GTD is not in causing the disease itself, but in determining a patient's capacity to successfully access and adhere to the demanding, long-term clinical management required for a cure. In essence, SES dictates the resources a woman has to *be a patient* with a complex condition.

The contradictory finding from Berkowitz et al. (1985), which identified an increased risk among women in "professional occupations," can be interpreted within this framework.[12] Rather

than SES itself being the risk factor, the occupation may be a proxy for a known biological risk: delayed childbearing. In 1985, women in professional careers were more likely to delay pregnancy into their late 30s and 40s, a well-established risk period for molar pregnancy (Ind et al., 2023; Lurain, 2010). Conversely, the descriptive data from LMICs showing high rates of GTD in poor populations may reflect the co-occurrence of other risk factors in these settings, such as nutritional deficiencies (e.g., low carotene intake) and higher parity (Al-Hussaini et al., 2019; Tadesse et al., 2025).

Potential Mechanisms and Biological Plausibility

The mechanisms through which SES influences GTD differ for risk and outcomes. For the potential, albeit weak, association with *risk*, the most biologically plausible pathway is through nutrition. Diets deficient in carotene and folic acid, which are more common in impoverished populations, have been linked to an increased risk of molar pregnancy (Ind et al., 2023; Tadesse et al., 2025). This provides a direct biological link between poverty and the abnormal fertilization events that characterize GTD.

For the much stronger association with *poor outcomes*, the mechanisms are overwhelmingly social and structural:

1. **Structural Barriers to Care:** Patients with low income, lack of reliable transportation, or those living in medically underserved areas face significant hurdles in accessing the specialized centers best equipped to manage GTD (Tadesse et al., 2025; Ndour et al., 2016). This leads to delayed diagnosis and initiation of treatment.
2. **Financial Toxicity and Non-Adherence:** The prolonged follow-up period, involving frequent and costly hCG tests for at least six months, is a significant financial burden (Moshfegh et al., 2023). For unemployed or uninsured women, the cost can be prohibitive, leading to premature discontinuation of surveillance. This is a critical failure point, as it prevents the timely detection of post-molar GTN. The high rates of loss to follow-up in low-income settings

(Gwala and Bhengu, 2019) are a direct manifestation of this mechanism.

3. **Lack of Social Support:** The robust findings from large database studies linking unmarried or widowed status to poorer survival highlight the importance of social capital (Liu et al., 2022; Zhang et al., 2023). A supportive partner can provide crucial emotional, logistical, and financial assistance throughout the arduous treatment journey. The absence of this support network can exacerbate psychological distress and negatively impact treatment adherence.
4. **Health Literacy:** Lower educational attainment, which is strongly correlated with low SES, may affect a patient's comprehension of the disease's nature and the absolute necessity of the long surveillance period after a molar evacuation, which can seem counterintuitive after the primary issue is surgically resolved (Aqsa et al., 2025; Islam and Bhowmik, 2024).

Strengths and Limitations of the Review

The primary strength of this review is its comprehensive and systematic approach to a question that has previously been addressed in a fragmented manner. By including studies from a wide range of global settings and explicitly distinguishing between risk and prognostic factors, it provides a novel and more nuanced understanding of the topic. The adherence to PRISMA guidelines and the use of a formal quality assessment tool enhance the transparency and rigor of the review.

However, the review is subject to several limitations inherent in the available literature. First, there is significant heterogeneity in the definition and measurement of SES across studies, ranging from validated scales to simple descriptive categories, which complicates direct comparisons. Second, many of the included studies, particularly from LMICs, were of lower methodological quality with a high risk of selection and confounding bias. Third, the potential for ecological fallacy exists in studies that use area-based measures of income (e.g., SEER data), which may not accurately reflect an individual patient's financial situation. Finally, there is a clear paucity of high-quality, prospective cohort studies specifically designed to investigate the impact of SES on GTD while controlling for all relevant confounders.

Implications for Clinical Practice and Public Health Policy

The findings of this review have significant implications for both clinical practice and broader health policy.

For Clinical Practice: Clinicians must recognize that socioeconomic factors are not just background information but are potent risk factors for adverse outcomes. Patients who are unemployed, unmarried, uninsured, or reside in deprived areas should be considered at high risk for non-adherence and treatment failure. Proactive implementation of support systems, such as patient navigation programs to assist with appointments and financial aid, integrated social work consultations, and the use of telehealth to reduce the travel burden for follow-up, could mitigate some of these barriers and improve adherence.

For Public Health Policy: At a systemic level, the findings underscore the need for targeted investment. In low-resource settings, establishing centralized GTD registries and dedicated treatment centers can improve the quality of care, concentrate expertise, and reduce the high rates of loss to follow-up (Gwala and Bhengu, 2019; Ndour et al., 2016). In high-income countries, policies must ensure that health insurance coverage is comprehensive enough to prevent the financial toxicity of long-term surveillance and potential chemotherapy from derailing treatment for this highly curable cancer. The finding by Liu et al. (2022) of better survival in rural locations in the US is counterintuitive but may suggest that for rare diseases, referral to and support from a limited number of high-volume centers of excellence is a more effective strategy than diffuse, lower-quality local care.

CONCLUSION AND RECOMMENDATIONS

Conclusion

This systematic review concludes that while the role of socioeconomic status as an independent etiologic risk factor for Gestational Trophoblastic Disease is ambiguous, SES emerges

as a powerful and significant determinant of clinical outcomes. Socioeconomic deprivation—manifesting as unemployment, lack of social support, and structural barriers to healthcare—critically undermines a patient's ability to complete the necessary long-term surveillance and treatment. This transforms a highly curable disease into a potentially fatal one, not because of its inherent biology, but because of the social and economic context in which the patient lives. The excellent prognosis of GTD can only be realized if patients have the socioeconomic resources to access and complete the full course of care.

Recommendations for Future Research

To address the limitations in the current evidence base and to inform the development of effective interventions, the following research is recommended:

1. **Prospective Cohort Studies:** There is an urgent need for well-designed, multicenter prospective cohort studies that use standardized, individual-level measures of SES. Such studies could more definitively clarify the role of SES in both the risk and prognosis of GTD, while carefully controlling for known confounders like maternal age, reproductive history, and nutritional status.
2. **Qualitative Research:** Qualitative studies are needed to explore the lived experiences of socioeconomically disadvantaged women with GTD. Understanding their perspectives on the specific barriers—be they financial, logistical, cultural, or educational—that lead to high rates of non-adherence is essential for designing patient-centered interventions.
3. **Health Economic Analyses:** Research is required to evaluate the cost-effectiveness of interventions aimed at improving adherence in at-risk populations. Studies analyzing the return on investment for programs like patient navigation, transportation vouchers, or subsidized childcare during appointments could provide a strong evidence base for policymakers to fund such initiatives.

REFERENCES

Al-Hussaini, T.K., Al-Kindi, R.M., and Al-Maniri, A.A. (2019). Epidemiology and management of gestational trophoblastic disease at a single tertiary care hospital in Oman. *Sultan Qaboos University Medical Journal*, 19(2), e129–e134.

Aqsa, Solangi, B., Jamali, S., Farah, Dhari, A., Channa, A., and Baloch, R. (2025). Rising Frequency of Gestational Trophoblastic Disease in Patients without Known Traditional Risk Factors: A Descriptive Cross-Sectional Study. *Journal of Mardan Medical Complex*, 16(1).

Berkowitz, R.S., Cramer, D.W., Bernstein, M.R., Cassells, S., Driscoll, S.G., and Goldstein, D.P. (1985). Risk factors for gestational trophoblastic neoplasia. *American Journal of Obstetrics and Gynecology*, 153(3), 323–326.

Cano Cárdenas, L.A., Morales-García, J.D.P., and Ávalos-Ríos, J.A. (2020). Risk factors associated with gestational trophoblastic disease at the National Hospital Hipólito Unanue. *Revista de la Facultad de Medicina Humana*, 20(1), 64-69.

de Freitas, S.G., Braga, A., Maestá, I., Elias, K.M., Horowitz, N.S., and Berkowitz, R.S. (2024). Molar Pregnancy: An Update on a Continuous Challenge. *Cancers*, 16(12), 2209.

Ebrahimzadeh, S., Janghorban, R., and Latifnejad, R. (2015). Investigation of Risk Factors, Stage and Outcome in Patients with Gestational Trophoblastic Disease since 2001 to 2011 in Iran-Yazd. *Global Journal of Health Science*, 7(5), 296–301.

Fairley, L., Allardice, G., Best, K., and Norman, J. (2021). Socio-economic inequalities in adverse pregnancy outcomes in a stable and developed population over 20 years: a population-based cohort study. *BMJ Open*, 11(3), e042753.

Guadamuz, J.S., et al. (2023). Study shows patients in low socioeconomic status neighborhoods

start cancer treatment later—and die sooner—than those in higher-status areas. *UC Berkeley Public Health*.

Gwala, M.L. and Bhengu, L. (2019). Gestational trophoblastic disease managed at Grey's Hospital, Pietermaritzburg, South Africa. *Southern African Journal of Gynaecological Oncology*, 11(2), 33-37.

Ind, T., et al. (2023). Gestational Trophoblastic Disease. *StatPearls Publishing*.

Islam, R., and Bhowmik, D.K. (2024). Profiling Molar Pregnancy: Demographic and Clinical Insights at a Tertiary Care Hospital in Bangladesh. *IOSR Journal of Dental and Medical Sciences*, 23(11), 71-77.

Khatun, M.S., Begum, F., Begum, M., and Ferdous, J. (2020). A Case-Control Study on Selected Maternal Risk Factors of Molar Pregnancy. *Journal of Preventive and Social Medicine*, 39(2), 34-39.

Liu, C., James, A., Wolf, J., Schmidt, M., et al. (2022). Analysis of the relationship between social determinants of health and survival outcomes in gestational trophoblastic neoplasia in the United States. *Journal of Clinical Oncology*, 40(16_suppl), e17537.

Lurain, J.R. (2010). Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. *American Journal of Obstetrics and Gynecology*, 203(6), 531-539.

Lurain, J.R. (2021). Gestational Trophoblastic Disease II: Classification and Management of Gestational Trophoblastic Neoplasia. *American Journal of Obstetrics and Gynecology*, 224(1), 40-52. [Corrected from 2020]

Madan, A., Soni, S., Upasana, Agrawal, K., and Neki, N.S. (2017). A Study on Incidence and

Clinical Profile of Gestational Trophoblastic Disease in a Tertiary Care Hospital. *International Journal of Contemporary Research in Medical Sciences*, 3(8), 2354-2357.

Moshfegh, A., et al. (2023). Gestational trophoblastic neoplasia development after normal human chorionic gonadotropin level following molar pregnancy: A systematic review and meta-analysis. *Obstetrics & Gynecology*, 141(5), 987-996.

Ndour, A.D., et al. (2016). Management of gestational trophoblastic neoplasia in a low-income country. *Obstetrics & Gynecology*, 127, 114.

O'Neill, K., and Guha, S. (2023). Racial disparities in early pregnancy: a narrative review. *Current Opinion in Obstetrics and Gynecology*, 35(Suppl 2), S1-S5.

Ou, S.H.I., et al. (2018). Socioeconomic Status and Lung Cancer Survival: A Systematic Review and Meta-Analysis. *Frontiers in Oncology*, 8, 536.

Palmer, J.R., Driscoll, S.G., and Rosenberg, L. (1999). Oral contraceptive use and risk of gestational trophoblastic tumors. *Journal of the National Cancer Institute*, 91(7), 635-640.

Petrelli, F., et al. (2022). Socio-Economic Inequalities in Lung Cancer Outcomes: An Umbrella Review. *Cancers*, 14(2), 398.

Rahman, M.M., et al. (2024). Impact of cancer diagnosis on life expectancy by area-level socioeconomic groups in New South Wales, Australia: a population-based study. *Cancer Biology & Medicine*.

Shaikh, F., Khan, T., and Kamran, R. (2013). Molar pregnancy: a review of 39 cases. *Journal of Ayub Medical College Abbottabad*, 25(1-2), 140-142.

Smith, H.O. (1996). Gestational trophoblastic disease. Epidemiology and etiology. *Obstetrics and Gynecology Clinics of North America*, 23(2), 211-229.

Tadesse, A., et al. (2025). Burden and predictors of gestational trophoblastic disease in East Africa: a systematic review and meta-analysis. *BMC Pregnancy and Childbirth*, 25(1), 1-12.

Tesfaye, T., et al. (2024). Prevalence and histopathological patterns of gestational trophoblastic disease in Africa: a systematic review and meta-analysis. *BMJ Open*, 14(5), e082260.

Weck, M.N., Paulose, T., and Flaws, J.A. (2008). Impact of environmental factors and poverty on pregnancy outcomes. *Clinical Obstetrics and Gynecology*, 51(2), 349-361.

Zhang, Y., et al. (2023). Clinical features and demographic characteristics of gestational trophoblastic neoplasia: Single center experience and the SEER database. *Cancer Medicine*, 12(15), 16409-16422.