ORIGINAL ARTICLE

ANNALS OF PUNJAB MEDICAL COLLEGE

Comparison of Risk Factors for Molar Pregnancy in PRIMI And Multi-gravid Women, A Comparative Cross-Sectional Study

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Submitted for Publication: 07-09-2025
Accepted for Publication 19-11-2025

How to Cite: Batool Z, Bano S. Comparison of Risk Factors for Molar Pregnancy in PRIMI And Multi-gravid Women, A Comparative Cross-Sectional Study. APMC 2025;19(4):335-339. **DOI: 10.29054/APMC/2025.1816**

ABSTRACT

Background: Molar pregnancy denotes a spectrum of abnormal placentation ranging from benign partial and complete hydatidiform mole to choriocarcinoma. Incidence varies worldwide, influenced by genetic, environmental, and socioeconomic factors. **Objective:** To compare the association of risk factors with molar pregnancies in PRIMI and multigravida women. **Study Design:** Comparative cross-sectional study. **Settings:** Obstetrics & Gynecology Department at Sahiwal Teaching Hospital, Sahiwal Pakistan. **Duration:** Two years (July 2023 to June 2025). **Methods:** 160 cases were included. Demographic and clinical parameters, including participants' age, gestational age at presentation, parity, and educational and socioeconomic status, were noted. **Results:** Of the 160 patients included, 70 were primigravida and 90 were multigravida. 70.0%, n=112, were 18–30 years with a mean age of 28.67 ± 3.87 years. The mean gestational age was 10.52 ± 1.54 weeks. Different risk factors noticed as 5.0% previous molar pregnancy, 46.3% poor socioeconomic status, 45.6% had blood group A, 20.0% prior abortion, 41.9% illiterate, 6.9% had age 35 years, and 35.0% had a history of oral contraceptive use. When compared between two groups, multiparous women had significantly more prior abortions as compared to primiparous (35.6% vs. 0.0%, $p < 0.001$); on the other hand, primiparous women were more illiterate as compared to multiparous (52.9% vs. 33.3%, $p = 0.013$). No significant differences were found among the remaining factors. **Conclusion:** Most of the risk factors did not differ significantly between the two groups. Sociodemographic factors may be more influential in determining risk.

Keywords: *Multigravida. Molar gestation, Primigravida, Contributing factors.*

INTRODUCTION

Molar pregnancy, or hydatidiform mole, is a gestational trophoblastic disorder caused by abnormal fertilization and may progress to gestational trophoblastic neoplasia (GTN).[1] In complete molar pregnancy, fetal tissue is absent. Abnormal placental tissue is present in the fetal portion of partial moles. Gestational Trophoblastic Neoplasia represents the malignant counterpart and entails invasive moles, Placental Site Trophoblastic Tumors, Epithelioid Trophoblastic Tumors, and choriocarcinoma.[2]

High around 100% cure rates can be achieved, and fertility can be preserved if timely diagnosis is made and suitable Multidisciplinary care is available.[3,4] Molar pregnancy has a wide range of prevalence worldwide, ranging from 0.3 to 16 per 1,000 pregnancies. Higher incidence is noted in Sindh, Iran, and Turkey.[5] It is about 0.5 to 1 per 1,000 pregnancies in North America and Europe, and around 2 per 1,000 in Southeast Asia. Even higher risk, detect them promptly, and ultimately plan suitable management. Many factors, such as the woman's age (advanced or younger, 35+ or 20-), ethnic background, nutritional status, socioeconomic level, and accessibility to healthcare facilities, contribute to its occurrence and detection.[6-9]

Age, therefore, appears to be an independent determinant of molar pregnancy, regardless of parity. A prior history of molar pregnancy substantially increases the risk of recurrence in future pregnancies.[8,10,11] Most molar pregnancies occur sporadically, but rare familial cases suggest a possible role for inherited genetic mutations in certain patients.[12] Other commonly reported

risk factors include multiparity, low socioeconomic status, illiteracy, and rural residence.[13] Genetic mutations, such as NLRP7 methylation defects and nutritional deficiencies, contribute to molar pregnancy, particularly recurrent cases.[14] Reproductive history and sociodemographic factors also play key roles. Khatun's study highlighted associations with young maternal age, blood group A, contraceptive use, illiteracy, and low socioeconomic status.[15] Multiple spontaneous abortions increase risk, with two or more linked to a threefold rise in complete moles and a twofold rise in partial moles.[8,10,16]

Low levels of carotene increase the risk of having molar gestations.[17] Extremes of maternal age, more than 45 and very young age, are known contributing factors for complete molar pregnancies.[18,19] It is debatable whether molar pregnancies are more common in primiparous or multiparous women, with variable citations in the existing literature.[3]

Our study is designed to identify specific contributory factors that can be modified in primiparous and multiparous women, given a gap in the literature and because this has not been explored, given the uncertainties in its etiology, especially in developing countries like Pakistan. This study addresses this gap by assessing the frequency and distribution of contributory factors among both groups, thereby advancing understanding of the epidemiology of molar pregnancy in our context.

METHODS

A cross-sectional study at the Department of Obstetrics & Gynecology, Sahiwal Teaching Hospital, for a period of 24 Months from 01-07-2023 to 30-06-2025 was conducted. A total of 160 patients presented with molar pregnancy during this time period.

Participants for the study were selected through non-probability consecutive sampling from women who presented to the gynecology department with suspected molar pregnancy. Women included were nulliparous or multiparous, aged between 18 and 45 years, with a gestational age of less than 14 weeks and a clinical or ultrasound-based diagnosis of molar pregnancy and raised beta HCG level, and confirmed histopathologic evidence of partial or complete mole. Only those who provided informed consent were enrolled. Women were excluded if there was no histopathological evidence of molar pregnancy, if beta-HCG levels were normal or ultrasound findings did not support the diagnosis, or if they declined to give informed consent.

After obtaining permission from the institutional ethical review committee (S. No. 105/IRB/SLMC/SWL, dated 15/06/2023), a Total of 160 women presenting to the Obstetrics and Gynecology outpatient and emergency departments at Sahiwal Teaching Hospital, fulfilling the inclusion criteria, were selected after obtaining informed consent from each woman. Baseline data, including age, gestational age, parity, educational status, and place of living, were noted. All the women underwent height and weight assessment for BMI. All patients were examined for contributing factors of molar pregnancy, including low socioeconomic status, smoking, history of oral contraceptive intake, history of any abortion, and blood type A, Illiteracy, prior molar pregnancy. All patients were managed according to unit protocol. All data obtained was recorded.

All data were entered in SPSS version 25. All qualitative variables, such as smoking, history of oral contraception use, prior molar pregnancy, low socio-economic history, blood type A, prior abortion, illiteracy, age < 20 and > 35 years, were presented as frequency and percentages. All quantitative measures, including age, gestational age, and BMI, were presented as mean ± S.D. Post-stratification Chi-square test was used for comparing the association of risk factors between primiparous and multiparous women, and a p-value ≤0.05 was taken as significant.

RESULTS

A Total of 160 patients fulfilling the inclusion and exclusion criteria were selected to determine the frequency of contributing factors associated with molar pregnancy (partial and complete) among multiparous and primiparous women. We found that out of 160 patients, 70 % (n=112) were in the age group of 18-30 years and 30% (n=48) were in the age group of 31-45 years. (Figure 1) Mean age was 28.67± 3.87 years, gestational age 10.52± 1.54 weeks, and BMI was 26.02± 3.50 kg/m2. (Figure: 2) Among the contributing factors studied, smoking was found 1.3 %(n=2), history of oral contraception used 35.0 %(n=56), prior molar pregnancy 5.0 %(n=8), low socio economic status 46.3 %(n=74), blood type A 45.6 %(n=73), prior abortion 20.0% (n=32), illiteracy 41.9 %(n=67), age < 20 & > 35 years was 6.9 %(n=11).

In this cohort of 160 women (70 primiparous, 90 multiparous), various risk factors were analyzed for association with parity using the Chi-square test. Two risk factors showed statistically significant differences, while the rest did not. Prior abortion is significantly more common in multiparous women. Maternal illiteracy is significantly more common in primiparous women. No significant differences were found for smoking, contraceptive use, molar pregnancy, socioeconomic status, blood group A, or age distribution. In comparing risk factors for molar pregnancy between primigravid (n=70) and multigravid women (n=90), most variables showed no statistically significant difference between the

two groups. The prevalence of smoking, prior molar pregnancy, low socioeconomic status, blood group A, extremes of maternal age >35 years, and oral contraceptive use did not differ meaningfully between the two groups ($p > 0.05$). However, two factors demonstrated significant associations with parity. A history of prior abortion was reported exclusively among multigravidas (35.6% vs. 0.0%, $p < 0.001$), suggesting that reproductive history may influence molar risk in this group. Conversely, maternal illiteracy was more common among primigravidas (52.9% vs. 33.3%, $p = 0.013$), highlighting the role of educational disadvantage as a potential contributing factor in first pregnancies.

Figure 1: Distribution of age, N= 160

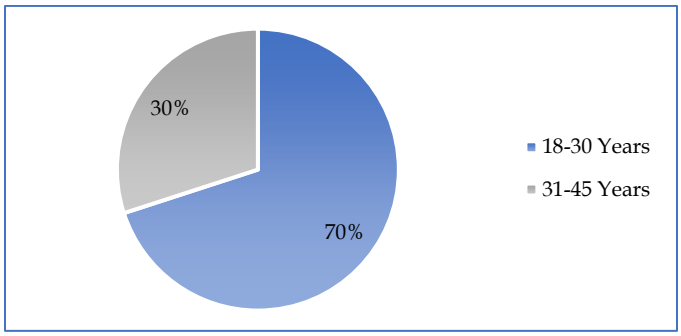

Figure 2: Mean & standard deviation of study variables

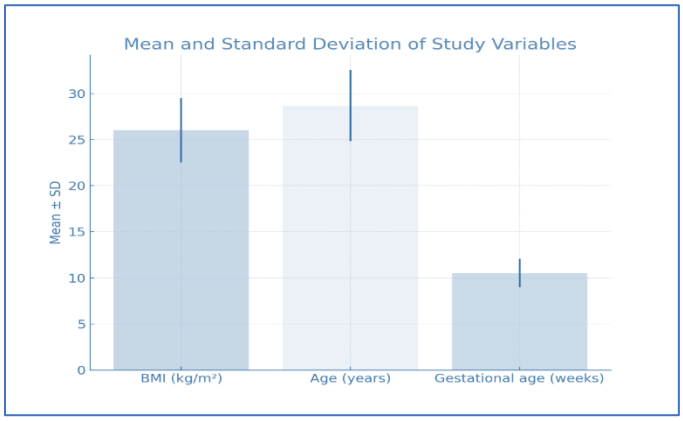

Table 1: Frequency distribution of risk factors (N = 160)

Risk Factor	Yes (n)	Yes (%)	No (n)	No (%)	Total
Smoking	2	1.3%	158	98.8%	160
Oral Contraceptive Use (History)	56	35.0%	104	65.0%	160
Prior Molar Pregnancy	8	5.0%	152	95.0%	160
Low Socioeconomic Status	74	46.3%	86	53.8%	160
Blood Type A	73	45.6%	87	54.4%	160
Prior Abortion	32	20.0%	128	80.0%	160
Maternal Illiteracy	67	41.9%	93	58.1%	160
Age <20 or >35 years	11	6.9%	149	93.1%	160

Table 2: Comparison of risk factors between nulliparous and multiparous women

Risk Factor	Primipara (n=70)	Multipara (n=90)	Total (N=160)	p-value	Significance
Smoking	1 (1.4%)	1 (1.1%)	2 (1.2%)	1.000	Not significant
Oral Contraceptive Use	28 (40.0%)	28 (31.1%)	56 (35.0%)	0.242	Not significant
Prior Molar Pregnancy	5 (7.1%)	3 (3.3%)	8 (5.0%)	0.299	Not significant
Low Socioeconomic Status	28 (40.0%)	46 (51.1%)	74 (46.2%)	0.162	Not significant
Blood Group A	32 (45.7%)	41 (45.6%)	73 (45.6%)	0.984	Not significant
Age <20 or >35 years	3 (4.3%)	8 (8.9%)	11 (6.9%)	0.350	Not significant
Prior Abortion	**0 (0.0%)**	**32 (35.6%)**	**32 (20.0%)**	**0.000**	**Significant (✓)**
Mother Illiterate	**37 (52.9%)**	**30 (33.3%)**	**67 (41.9%)**	**0.013**	**Significant (✓)**

DISCUSSION

Global studies have reported wide variations in the incidence of hydatidiform mole, influenced by diverse environmental risk factors. In Pakistan, one study showed 28 per 1000 incidence.[19] Mother's age, previous abortion, history of previous mole, ethnicity, history of OCP, blood group, socioeconomic status, and gene mutations have been reported as risk factors for the occurrence of HM.[8,10-18]

Among 160 women with molar pregnancy, in our study, 70.0% (n=112) were aged 18–30 years and 30.0% (n=48) were 31–45 years (mean age 28.67 ± 3.87 years). Extreme maternal age (35 years) is a recognized risk factor for molar pregnancy, with the greatest risk in women under 20 and particularly over 45 for complete moles.[8,12] A large analysis of 7,916 cases confirmed a significantly higher risk at age ≤15 and ≥45.[18,20] In our cohort, only 6.9% fell into this high-risk stratum, with a mean age of 28.67 years. This aligns with Pakistani studies by Fatima S,31.15±7.41 years and Iftikhar, 30.8±6.6 years.[13,21] Indian reports by Nalini, Seema, Jathwani, peak age is at 20–30 years.[22,23,24] By contrast, Khatun in Iran found 48% of cases below 20 years.[15] while Japanese data identified older maternal age (≥40) as a major determinant of incidence and adverse outcomes.[25,26] Regional variation is further illustrated by Al-Sharif in Yemen, where incidence peaked at 20–29 years.[27] This suggests our population trends for maternal age show few elderly and younger age mothers. To accurately interpret these findings, comparative controls must be studied.

The mean gestational age at diagnosis of molar pregnancy in our study is 10.52 ± 1.54 weeks. It correlates with the existing literature. Nalini reported 12.8 ± 2 weeks

of gestation in 66% of molar pregnancies at diagnosis.[22] Iftikhar in Pakistan likewise reported a diagnosis at 13.3 ± 2.[21] The use of early ultrasound aids the detection of cases earlier.

20.0% of women had a prior abortion in our study. It is lower than mentioned in the literature, but it has significance. Benirschke mentioned a threefold increased risk for complete mole and a twofold increased risk for partial mole in women with recurrent miscarriages.[17] Iftikhar in Pakistan mentioned a very high prevalence of 69.2% after prior pregnancy loss.[21] Several international studies favor this occurrence.[8,10,27]

Blood group A was more frequent in our study. But the role of blood group is not mentioned in the current studies. It could be just a chance finding.[15, 27] Smoking was present in 1.3% in our population. Milani mentioned 7% smokers a study, a higher percentage than ours.[28] The literature does not describe the relationship of smoking with molar pregnancies.

Our study reveals 5.0% of women with prior molar pregnancy. It correlates with the previous studies, which confirm an elevated risk associated with a prior mole. Kashanian reported an odds ratio of 5.7 with a prior mole, and Khatun mentioned 4% recurrence risk after one molar pregnancy.[8,15] Multiple series have documented this association, including links between prior first-trimester loss and current molar diagnosis.[10,29] Prospective data also suggest that a history of molar pregnancy predicts subsequent development of post-molar trophoblastic neoplasia.[29] Overall, recurrence risk is estimated at ~1% after one mole and rises sharply to 15–20% after two or more by one analysis.[30] A prior molar pregnancy, though infrequent, is a significant risk factor that necessitates vigilant surveillance and structured follow-up.

In our study, 46.3% of women belonged to a low socioeconomic group, and 41.9% were illiterate. Illiteracy and primary-level education were more common among primiparous than multiparous women. Poor nutrition, low socioeconomic status, and micronutrient deficiencies are frequently cited as risk factors for molar pregnancy, though their impact varies by region.[13,14,21,23,24,31] A case-control study in White women linked low carotene intake with increased risk, while higher intake was protective.[2] Regional studies show a consistent association with disadvantaged backgrounds. In Pakistan, Fatima *et al*. reported low socioeconomic status, limited education, and rural residence as common factors.[13] Indian studies similarly found high prevalence among women from poor households by Nalini, 70.7%; Seema Dayal, 74%; Jathwani, 54% from the poor socioeconomic group.[22,23,24] Comparable findings were reported in Iran, where Khatun noted 57.9% illiterate and 67% poor [15,] and in Bangladesh, where Akhter observed 63.9% illiterate and 73% from low socioeconomic groups.[31] All this explains the association of poverty, poor diet, and awareness, and lower utilization of healthcare facilities in these areas.

In our study, oral contraceptive use was reported in 35% of women. The literature suggests inconsistent evidence for its association as a risk factor for molar pregnancy,[10,21,15,27] It might present the local contraceptive trends rather than causation in actuality.

There was uniform distribution of risk factors like maternal age, prior molar pregnancy, blood group A, and oral contraceptive use, associated with molar gestations between nulliparous and multiparous ladies in our study. It clarifies these as general factors and not parity-associated. Studies by Fatima *et al*. and Alimohammadi have reported multiparty as a significant factor for molar gestations.[10,13] Our study poses a stronger impression of sociodemographic factors. We observed a previous abortion only among multiparous women. It explains that uterine trauma or endometrial changes after a miscarriage or induced abortion can lead to abnormal trophoblastic implantation. On the other hand, primiparous women were more illiterate, which reflects the contribution of poor education to late presentation, undernourishment, and a scarce health-seeking attitude in these women. This highlights that parity alone is not affect the occurrence of molar gestations. Risk factors for molar are shaped by sociodemographic factors.

CONCLUSION

Our findings show uniform distribution of risk factors for molar pregnancies among multiparous and nulliparous ladies. Poor socioeconomic level and lower educational status in the primiparous women are highlighted as major contributory factors for molar pregnancy in our study. It supports the nutritional deficiency and regional variation in the occurrence. A history of molar pregnancy and miscarriage was noticed as a moderate risk factor and was more common in multiparous women. Extremes of maternal age were less frequent as compared to reported in the literature. To conclude, molar gestations are affected by intricate involvement of genetics and sociodemographic variables, highlighting the need for multi-centre research for the provision of preventive and early diagnostic approaches.

LIMITATIONS

There was no unaffected control group in the study cohort for true representation.

SUGGESTIONS / RECOMMENDATIONS

Further research is required where population-based controls are added, proper dietary assessment is taken,

access to healthcare facilities is noted, and environmental exposures are established to draw strong conclusions.

CONFLICT OF INTEREST / DISCLOSURE

None.

ACKNOWLEDGEMENTS

Abdullah Farooq, a first-year medical student, for helping with graphics and tables

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