# Role Of GATA3 Expression In Trophoblastic Tissue

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## ABSTRACT

**Objectives**: This study aimed to know the expression of GATA-3 in trophoblastic tissues and to explore its utility in confirmation of uncertain histopathological diagnosis.

**Materials and methods**: It was a cross sectional study conducted in 2021 in a south Indian district in a tertiary care hospital from public sector. Around 64 specimens were taken up or the study. Specimen collection involved receiving samples in 10% formalin, followed by fixation in fresh formalin for 24 hours. Gross descriptions, reports of Hematoxylin and eosin staining were documented, followed by immunohistochemistry. GATA 3 IHC was performed on paraffin-embedded tissue specimens. For a positive result, nuclear expression within trophoblastic cells was required. This process ensured accurate assessment of GATA3 expression in trophoblastic tissues.

**Results**: Mean (SD) age was 25.86 (5.52) years. GATA3 expression was negative for all 3 trophoblasts only for 1 case (1.6%). In a study of 64 specimens, all 56 consistent with products of conception showed 100% GATA3 expression in intermediate trophoblast and cytotrophoblast tissues, but only 20.4% displayed GATA3 expression in syncytiotrophoblast tissue. In 5 specimens identified as Hydatidiform mole, all showed 100% GATA3 expression in intermediate trophoblast and cytotrophoblast, with none showing GATA3 expression in syncytiotrophoblast tissue. If GATA3 expression is more pronounced in one trophoblast subtype, it is likely to also be more pronounced in the other trophoblast subtype, and the reverse holds true as well.Expression of GATA-3 expression was noted in trophoblastic tissues in > 98% specimen.

**Conclusion**: The study cannot approve completely of its utility in confirmation of uncertain histopathological diagnosis.

**Keywords**: GATA-3 expression, Immunohistochemistry, Trophoblast, Pregnancy, Unsafe abortion.

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## 1. Introduction

GATA-3 is a zinc-finger transcription factor with a wide variety of functions, including the development and differentiation of breast tissue, the urothelial/ renal systems, T-cell lymphocytes, skin, and parts of the nervous

system.[1] It also plays a significant role in embryogenesis, including the development of trophoblastic tissues, and it can have implications for maternal health and mortality.[2]

GATA-3 is involved in the early stages of embryonic development. It plays a crucial role in the formation of the trophoblast, which is a tissue that surrounds the developing embryo. The trophoblast is essential for implantation in the uterus and the subsequent development of the placenta. GATA-3 is involved in regulating the genes necessary for proper trophoblast differentiation, its maintenance and function. In embryonic stem cells, GATA3 can supersede pluripotency and steer the activation of numerous genes associated with trophoblastic development. Meanwhile, in trophoblastic stem cells, GATA3 plays a dual role in driving differentiation. It accomplishes this by independently initiating the expression of trophoblast-specific genes and working in harmony with other regulators of placental development, such as CDX2.[(3-5)] GATA-3 dysregulation or mutations can have implications such as preeclampsia, placental abnormalities, fetal growth restriction, and miscarriages.

In this regard, active researches are conducted to improve our understanding of these processes and develop strategies for early detection and intervention to improve maternal and fetal outcomes. GATA3 expression may be studied prenatally using Non-invasive prenatal testing (NIPT), advanced imaging techniques etc. However, in current context, the focus is on studying GATA-3 expression in conception products after abortion. Reasons being, the estimate that nearly 25 million unsafe abortions occur each year world-wide, leading to approximately 22,000 maternal deaths.[6] In India, despite the legislative protection with the historic Medical Termination of Pregnancy Act of 1971, unsafe abortion remains the third leading cause of maternal mortality in India, and close to 8 women die from causes related to unsafe abortion each day.[7]

Unsafe abortions and its consequences are potential medicolegal cases; and in such cases histopathological diagnosis of specimen is of utmost value. The expression of the GATA3 gene in tissues after an abortion can vary depending on several factors, including the stage of pregnancy, the reason for the abortion, and the specific tissues being studied.

Understanding the specific roles of GATA3 in different trophoblast subtypes is essential for gaining insights into placental biology and improving the management of pregnancy-related conditions.[2,3]Research in this area can provide insights into the molecular changes that occur in the uterus and related tissues following an abortion. However, it's important to note that the available research may be limited, and the expression patterns of GATA3 can be complex and context-dependent. Hence the study was planned.

## 2. Materials & Methods

**2.1 Study setting:** Department of Pathology, KR District Hospital affiliated to Mysore Medical College and Research Institute, Mysuru, Southern India. Study for One calendar year i.e. January 2021 to December 2021.It was across-sectional study.Women in reproductive age group who conceived and whose specimen were sent to the Department of Pathology, KR District Hospital.

**2.2 Specimen collection and staining**: The specimens were received in 10% formalin, and after scrutinizing the patient details, the autopsy specimens were fixed in fresh formalin for 24 hours. Gross descriptions of all the fragments were documented, and processing was completed. Hematoxylin and eosin staining were applied to the sections, followed by confirmation using immunohistochemistry. Each stained section was assessed for the presence or absence of products of conception, and GATA 3 IHC staining was subsequently performed.

**2.3 Immunohistochemistry**:

Immunohistochemistry (IHC) for GATA3 was conducted using the appropriate antibodies on tissue specimens that were formalin-fixed and paraffin-embedded. GATA3 IHC utilized a prediluted mouse monoclonal antibody from Biocare Medical. To be deemed positive, the

tissue needed to exhibit nuclear expression within individual trophoblastic cells, including cytotrophoblast, intermediate trophoblast, and syncytiotrophoblast.

**2.4 GATA3 score**: Scoring of GATA3 immunostaining is semiquantitative. GATA3 labelling was scored on a scale of 0 to 4+ with the extent of nuclear staining graded as follows, [9]

**2.4.1** 0 (0–5%),
**2.4.2** 1+ (5%–24%),
**2.4.3** 2+ (25%–49%),
**2.4.4** 3+ (5o%–74%),
**2.4.5** 4+ (>75%)

For the purpose of statistical analysis, we categorized GATA3 staining as either negative (scored as 0) or positive (scored as 1+ or higher). The staining intensity was documented independently as weak, moderate, or strong. Any staining with an intensity exceeding 5% distribution was classified as positive.

**3 Statistical analysis:**

The information has been inputted as data into a Microsoft Excel Spreadsheet. Analysis was conducted using the trial version of SPSS software version 26.0. The findings are presented through tables and relevant diagrams. Quantitative data are summarized by providing the mean and standard deviation, whereas qualitative data are presented as proportions. The correlation between various groups for qualitative variables will be examined using either Pearson's chi-square test or by determining correlation co-efficient with the help of scatter graph. A p-value of less than / equal to 0.05 will be regarded as indicating statistical significance.



## 4. RESULTS

**Table 1: Age distribution of study participants**

| Age group | Frequency | Percentage |
|---|---|---|
| ≤ 20 years | 8 | 12.5 % |
| 21 – 25 years | 25 | 39.1 % |
| 26 – 30 years | 21 | 32.8 % |
| > 30 years | 10 | 15.6 % |
| **Total** | **64** | **100.0 %** |
| Mean (SD): 25.86 (5.52) years | | |

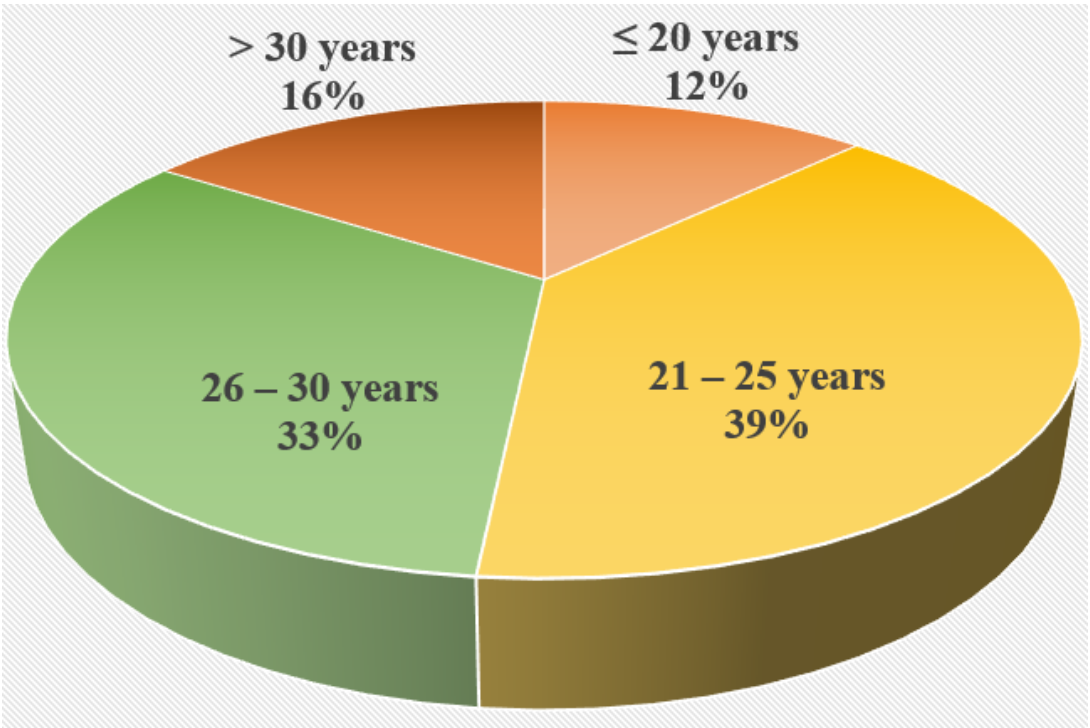

**Figure 1: Age distribution of study participants: Pie chart**

A total of 64 patients were taken up for the study. Mean (SD) age of the women (Table 1 / Figure 1) was 25.86 (5.52) years with 39% women in the age group of 21-25 years followed by 33% women in the age group of 26-30 years. Sources of trophoblast specimen (Table 2 / Figure 2) were from products of conception (54.7%), utero-cervix (25.0%) and ectopic sites (20.3%). Specimen was from the uterus in around four-fifths (79.7%) of the pregnant women (Table 3 / Figure 3).

**Table 2: Type of specimen**

| Type of specimen | Frequency | Percentage |
|---|---|---|
| POC | 35 | 54.7 % |
| Utero-cervix | 16 | 25.0 % |
| Ectopic | 13 | 20.3 % |
| **Total** | **64** | **100.0 %** |



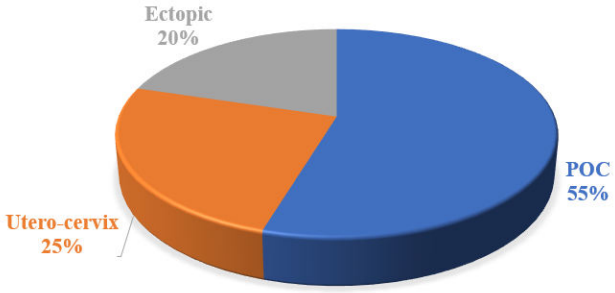


**Figure 2: Type of specimen: Pie chart**

**Table 3: Site of specimen**

| Site of specimen | Frequency | Percentage |
|---|---|---|
| Uterus | 51 | 79.7 % |
| Right fallopian tube | 8 | 12.5 % |
| Left fallopian tube | 5 | 7.8 % |
| **Total** | **64** | **100.0 %** |

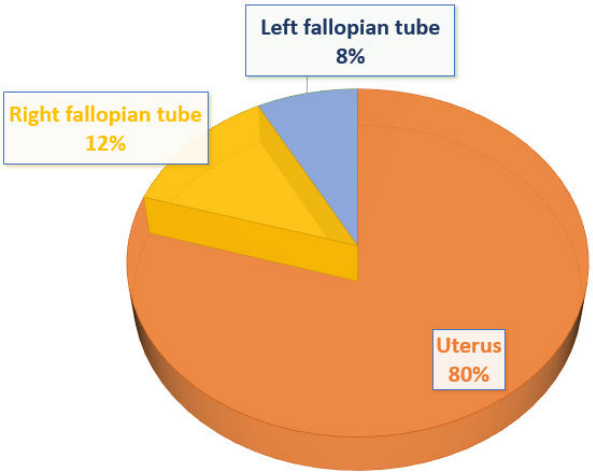


**Figure 3: Site of specimen: Pie chart**

**Table 4: Provisional diagnosis**

| Provisional diagnosis | Frequency | Percentage |
|---|---|---|
| Consistent with POC | 56 | 87.5 % |
| Hydatidiform mole | 5 | 7.8 % |
| Degenerated villi? | 2 | 3.1 % |
| Consistent with EP | 1 | 1.6 % |
| **Total** | **64** | **100.0 %** |

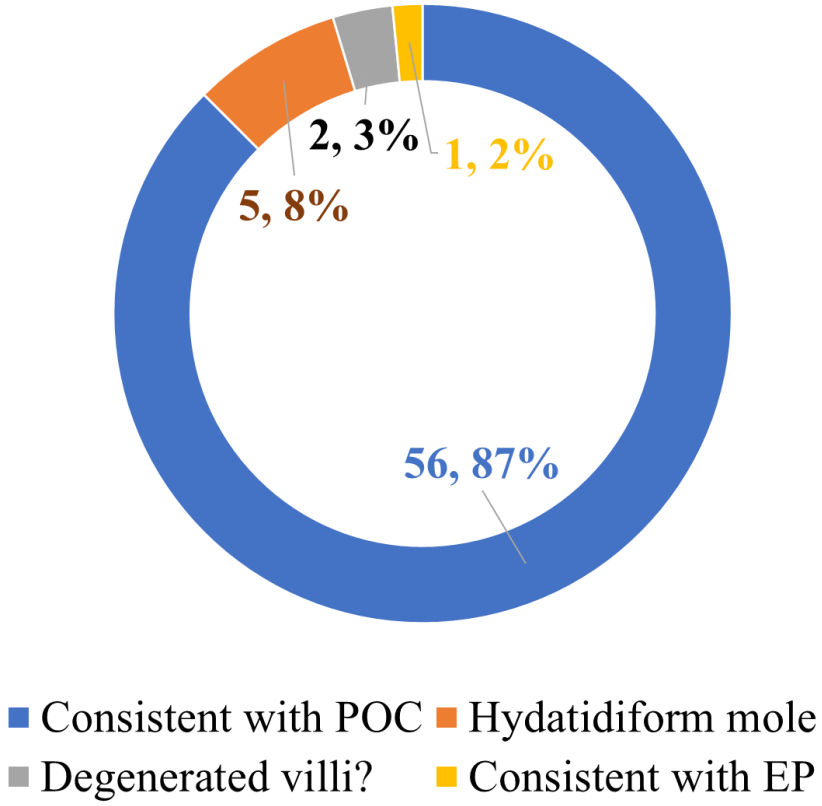


**Figure 4: Provisional diagnosis: Pie chart**

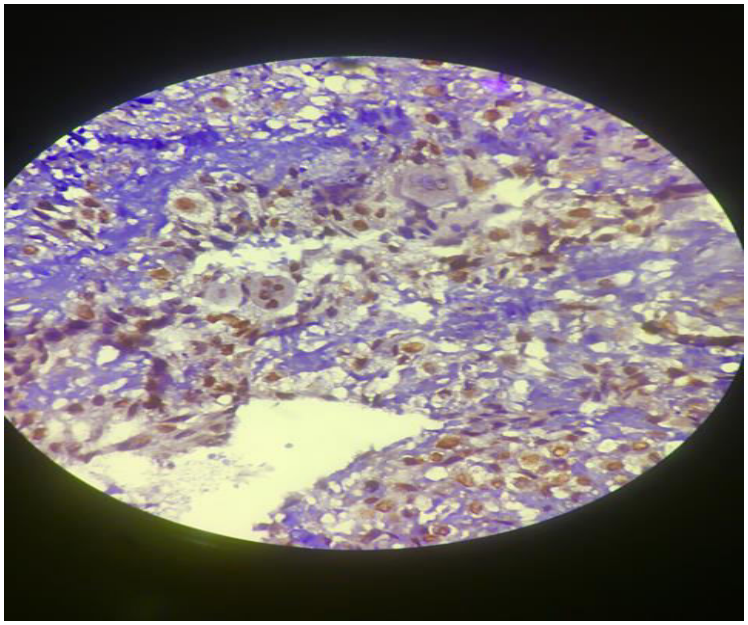

Figure 6: Ectopic Pregnancy: Cytotrophoblast and intermediate Trophoblast shows diffuse positivity, Syncytiotrophoblast shows moderate positivity.



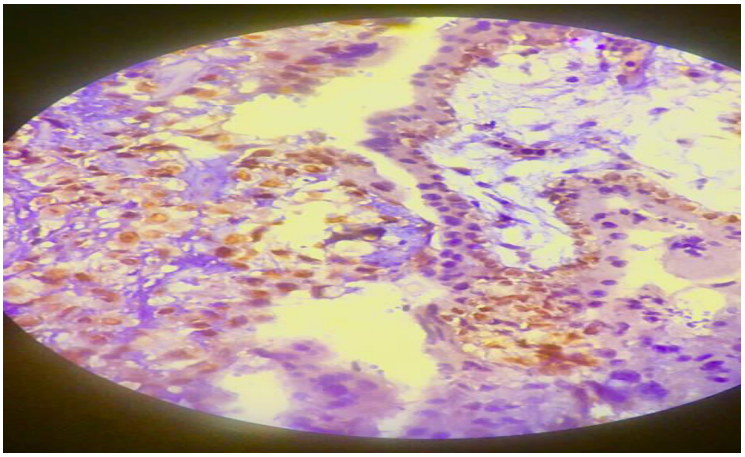

Figure 7: Ectopic Pregnancy: The cytotrophoblast and villous trophoblastic columns show diffuse strong expression. The syncytiotrophoblast are negative.

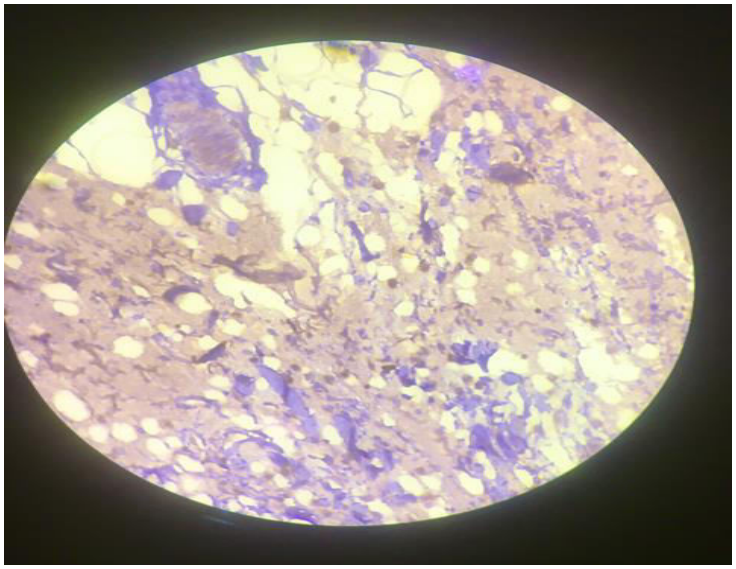



Figure 8: ? Degenerated villi section confirmed by GATA3 staining showing scattered GATA3 positive cytotrophoblasts.

As for provisional diagnosis (Table 4 / Figure 4), 87.5% specimen were consistent with products of conception followed by 7.8% specimen, which were of Hydatidiform mole, 3.1% were degenerated villi and 1.6% were consistent with ectopic pregnancy.

Table 5A and 5B explores in detail the expression of GATA3 using Immunohistochemistry scores. IHC scores for different trophoblast tissues were as below: Intermediate trophoblast IHC score ranged from 0 to 4 with a mean (SD) of 3.06 (0.64). Most i.e. 76.6% were of grade 3 followed by 17.2% which were of grade 4. Cytotrophoblast IHC score ranged from 0 to 3 with a mean (SD) of 1.83 (0.61). Most i.e. 70.3% were of grade 2 followed by 18.8% which were of grade 2. Syncytiotrophoblast IHC score ranged from 0 to 2 with a median of 0. Most i.e. 79.7% were negative while 18.8% were of grade 1 & the remaining 1.6% were of grade 2.

**Table 5A: Immunohistochemistry (IHC) scores of various trophoblasts**

| IHC score | Frequency (N=64) | Percentage |
|---|---|---|
| **Intermediate trophoblast IHC score** | | |
| 0 | 1 | 1.6 % |
| 1 | 1 | 1.6 % |
| 2 | 2 | 3.1 % |
| 3 | 49 | 76.6 % |
| 4 | 11 | 17.2 % |
| **Cytotrophoblast IHC score** | | |
| 0 | 2 | 3.1 % |
| 1 | 12 | 18.8 % |
| 2 | 45 | 70.3 % |
| 3 | 5 | 7.8 % |
| **Syncytiotrophoblast IHC score** | | |
| 0 | 51 | 79.7 % |
| 1 | 12 | 18.8 % |
| 2 | 1 | 1.6 % |

**Table 5B: Summary measures of IHC scores of various trophoblasts**

| | Intermediate trophoblast | Cytotrophoblast | Syncytiotrophoblast |
|---|---|---|---|
| Range | 0 – 4 | 0 – 3 | 0 – 2 |
| Mean | 3.06 | 1.83 | 0.22 |
| Standard deviation | 0.64 | 0.61 | 0.45 |
| Standard error | 0.08 | 0.08 | 0.06 |
| Median | 3.00 | 2.00 | 0.00 |

**Table 6A: Frequency of GATA-3 expression in different diagnosis**

| Provisional diagnosis | Total cases | Positive GATA-3 expression [Frequency (Row percentage)] | | |
|---|---|---|---|---|
| | | Intermediate trophoblast | Cytotrophoblast | Syncytiotrophoblast |
| Consistent with POC | 56 | 56 (100.0%) | 56 (100.0%) | 12 (20.4%) |
| Hydatidiform mole | 5 | 5 (100.0%) | 5 (100.0%) | 0 |
| Degenerated villi? | 2 | 1 (50.0%) | 0 | 0 |
| Consistent with EP | 1 | 1 (100.0%) | 1 (100.0%) | 1 (100.0%) |



Table 6 shows the proportion of GATA3 expression in different scenarios. For the specimen which were consistent with products of conception (56 of 64), all 56 (100%) were positive for GATA3 expression in the tissues of intermediate trophoblast and cytotrophoblast, while only one-fifths i.e. 20.4% were positive for GATA3 expression in syncytiotrophoblast tissue. For the specimen which were that of Hydatidiform mole (5 of 64), all 5 (100%) were positive for GATA3 expression in the tissues of intermediate trophoblast and cytotrophoblast, while all were negative for GATA3 expression in syncytiotrophoblast tissue.

**Table 6B: Summary measures of IHC scoring for different diagnosis**

| | Intermediate trophoblast | Cytotrophoblast | Syncytiotrophoblast |
|---|---|---|---|
| CONSISTENT WITH POC (N=56) | | | |
| Range | 2 – 4 | 1 – 3 | 0 – 2 |
| Mean | 3.13 | 1.88 | 0.23 |
| Standard deviation | 0.43 | 0.51 | 0.47 |
| Standard error | 0.06 | 0.07 | 0.06 |
| Median | 3.00 | 2.00 | 0.00 |
| HYDATIDIFORM MOLE (N=5) | | | |
| Range | 1 – 4 | 1 – 2 | 0 |
| Mean | 3.40 | 1.80 | 0 |
| Standard deviation | 0.55 | 0.45 | 0 |
| Standard error | 0.25 | 0.20 | 0 |
| Median | 3.00 | 2.00 | 0 |
| DEGENERATED VILLI (N=2) | | | |
| Range | 0 – 1 | 0 | 0 |
| Mean | 0.50 | 0 | 0 |

| | | | |
|---|---|---|---|
| Standard deviation | 0.71 | 0 | 0 |
| Standard error | 0.50 | 0 | 0 |
| Median | 0.50 | 0 | 0 |
| CONSISTENT WITH EP (N=1) | | | |
| Range | NA | | |
| Mean | | | |
| Standard deviation | | | |
| Standard error | | | |
| Median | | | |

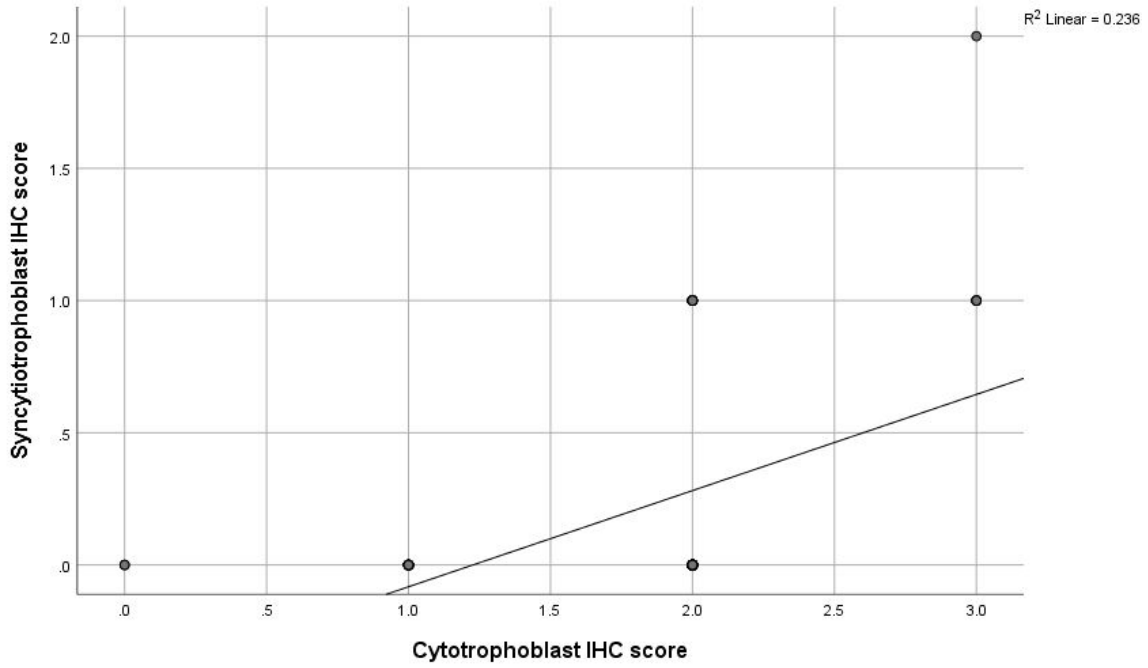


**Figure 5A: Correlation between Syncytiotrophoblast and Cytotrophoblast IHC score [Spearman's rho correlation co-efficient: 0.486; Co-efficient of determination: 0.236; p value: <0.001 (S)]**

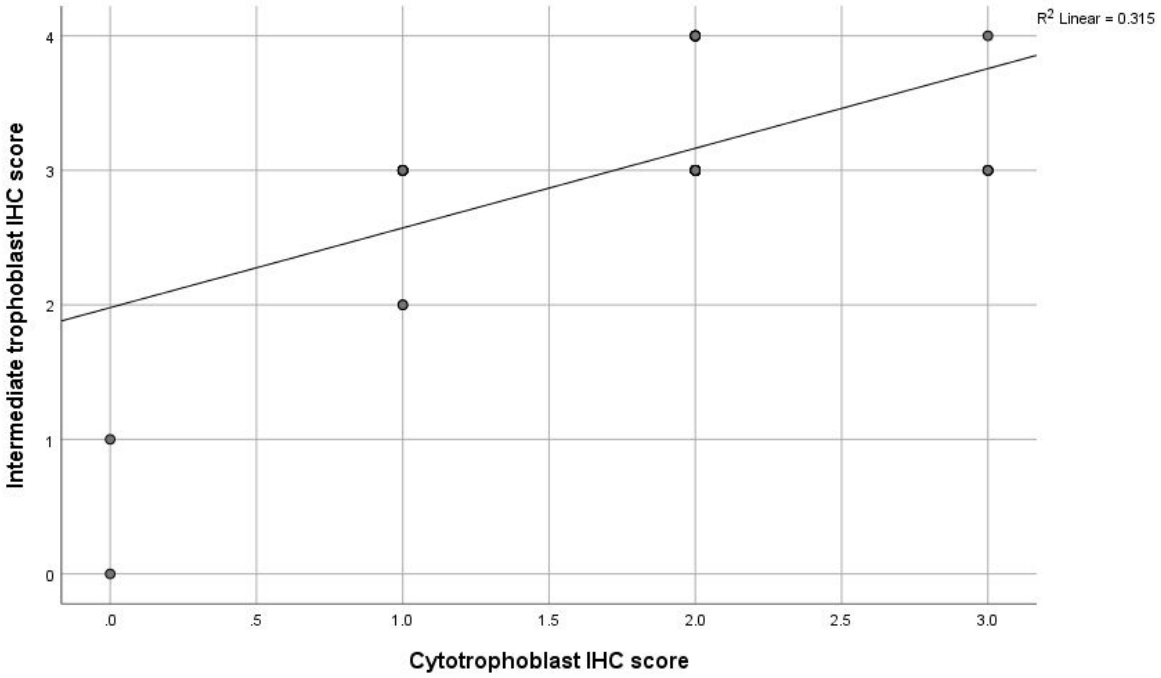


**Figure 5B: Correlation between Intermediate trophoblast and Cytotrophoblast IHC score [Spearman's rho correlation co-efficient: 0.398; Co-efficient of determination: 0.315; p value: 0.001 (S)]**



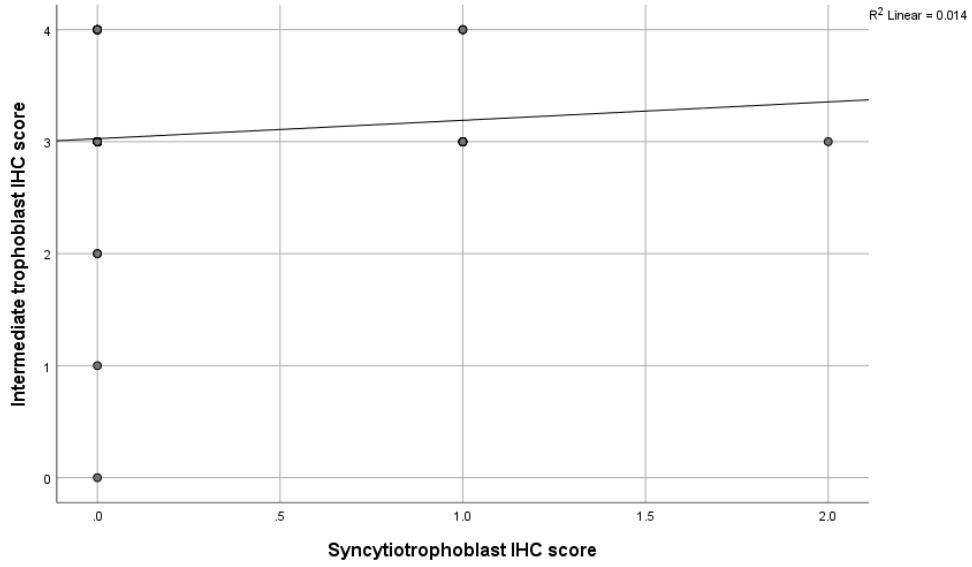


**Figure 5C: Correlation between Intermediate trophoblast and Syncytiotrophoblast IHC score [Spearman's rho correlation co-efficient: 0.122; Co-efficient of determination: 0.014; p value:** 0.34 (NS)]

Figure 5 shows correlation of GATA3 expression and its strength of positivity in different trophoblasts. Strongest correlation is observed between intermediate trophoblast and cytotrophoblast with correlation co-efficient of 0.398 followed by the correlation between syncytiotrophoblast and cytotrophoblast with correlation co-efficient of 0.236. Both of these correlations were statistically significant in the present study. Weakest and nonsignificant correlation was between intermediate trophoblast and syncytiotrophoblast.

**Table 7A: Association between IHC scores of Intermediate trophoblast & Cytotrophoblast**

| **Intermediate trophoblast IHC score** | **Frequency (Column percentage)** | | | | |
|---|---|---|---|---|---|
| | **Cytotrophoblast IHC score** | | | | |
| | **0** | **1** | **2** | **3** | **Total** |
| 0 | 1 (50.0%) | 0 | 0 | 0 | **1 (1.6%)** |
| 1 | 1 (50.0%) | 0 | 0 | 0 | **1 (1.6%)** |
| 2 | 0 | 2 (16.7%) | 0 | 0 | **2 (3.1%)** |
| 3 | 0 | 10 (83.3%) | 35 (77.8%) | 4 (80.0%) | **49 (76.6%)** |
| 4 | 0 | 0 | 10 (22.2%) | 1 (20.0%) | **11 (17.2%)** |
| **Total** | **2 (100.0%)** | **12 (100.0%)** | **45 (100.0%)** | **5 (100.0%)** | **64 (100.0%)** |
| Pearson's Chi-square test: $\chi^2$: 75.379, df: 12, **p value < 0.001 (S)** | | | | | |

**Table 7B: Association between IHC scores of Intermediate trophoblast & Syncytiotrophoblast**

| **Intermediate trophoblast IHC score** | **Frequency (Column percentage)** | | | |
|---|---|---|---|---|
| | **Syncytiotrophoblast IHC score** | | | |
| | **0** | **1** | **2** | **Total** |
| 0 | 1 (2.0%) | 0 | 0 | **1 (1.6%)** |
| 1 | 1 (2.0%) | 0 | 0 | **1 (1.6%)** |
| 2 | 2 (3.9%) | 0 | 0 | **2 (3.1%)** |
| 3 | 39 (76.5%) | 9 (75.0%) | 1 (100.0%) | **49 (76.6%)** |
| 4 | 8 (15.7%) | 3 (25.0%) | 0 | **11 (17.2%)** |
| **Total** | **51 (100.0%)** | **12 (100.0%)** | **1 (100.0%)** | **64 (100.0%)** |
| Pearson's Chi-square test: $\chi^2$: 1.760, df: 8, **p value < 0.001 (S)** | | | | |



**Table 7C: Association between IHC scores of Intermediate trophoblast & Cytotrophoblast**

| **Syncytio trophoblast IHC score** | **Frequency (Column percentage)** | | | | |
|---|---|---|---|---|---|
| | **Cytotrophoblast IHC score** | | | | |
| | **0** | **1** | **2** | **3** | **Total** |
| 0 | 2 (100.0%) | 12 (100.0%) | 37 (82.2%) | 0 | **51 (79.7%)** |
| 1 | 0 | 0 | 8 (17.8%) | 4 (80.0%) | **12 (18.8%)** |
| 2 | 0 | 0 | 0 | 1 (20.0%) | **1 (1.6%)** |
| **Total** | **2 (100.0%)** | **12 (100.0%)** | **45 (100.0%)** | **5 (100.0%)** | **64 (100.0%)** |
| Pearson's Chi-square test: $\chi^2$: 29.197, df: 6, **p value < 0.001 (S)** | | | | | |

Table 7 shows categorically the association between GATA3 expression and its strength of positivity in different trophoblasts. It showed that all the types of trophoblasts are significantly associated with each other. That is, if GATA3 expression is of higher grade in one type of trophoblast, then it the gene expression will be of higher grade in other type of trophoblast as well; and vice versa.

## 5. DISCUSSION

The present study was conducted with the objective to study the expression of GATA-3 in trophoblastic tissues and to explore its utility in confirmation of uncertain histopathological diagnosis. Mean age of 64 women included in the study was 25.8 years. Information regarding order or trimester of pregnancy, maternal outcome, mode of termination of pregnancy etc. could not be obtained, just like in most medicolegal cases.

On immunohistochemistry analysis in the present study, only 1.6% cases did not express GATA3 while all others expressed GATA3 at least in one of the trophoblasts. Around one-fifths (13 / 64 i.e. 20.4%) expressed GATA3 in all 3 types of trophoblasts. Furthermore, in

the study, among specimens consistent with products of conception (56 out of 64), GATA3 expression was found to be 100% positive in intermediate trophoblast and cytotrophoblast tissues. However, only 20.4% showed positive GATA3 expression in syncytiotrophoblast tissue. In specimens identified as Hydatidiform mole (5 out of 64), GATA3 expression was 100% positive in intermediate trophoblast and cytotrophoblast tissues, while it was entirely negative in syncytiotrophoblast tissue.

A study conducted by Banet N et al. in 2015 examined GATA-3 expression in various trophoblastic tissues and tumors (n=445) to address this gap. It was observed that developing trophoblasts and non-neoplastic trophoblastic proliferations, along with 81% of trophoblastic neoplasms, exhibited GATA-3 positivity. Expression levels varied among trophoblast cell types, with intermediate trophoblast consistently showing strong expression, whereas cytotrophoblast and syncytiotrophoblast expression decreased with advancing gestational age. Additionally, GATA-3 was found in 89% of normal/exaggerated implantation sites and 55% of placental site nodules. It was also detected in 78% of choriocarcinomas, 95% of epithelioid trophoblastic tumors, and 71% of placental site trophoblastic tumors. This study highlights the importance of recognizing GATA-3 expression in trophoblastic tumors to avoid misdiagnosis, especially when differentiating them from metastatic bladder or breast carcinomas. In challenging cases, GATA-3 can be a valuable addition to the immunohistochemical panel.[8]

Another study conducted by Mirkovic J et al. in 2015 reported following findings: In immature placentas, GATA3 staining was notably intense and widespread in the implantation site, specifically in the intermediate trophoblast and cytotrophoblast layers, with varying levels of staining in the syncytiotrophoblast layer Conversely, mature placentas exhibited reduced GATA3 expression, with sporadic positive staining in villous cytotrophoblast cells and minimal to no GATA3 expression in syncytial knots. The amnion layer consistently displayed GATA3 positivity, as did the intermediate trophoblast cells associated with fibrin present in both the chorionic plate and intervillous spaces. Notably, the implantation site in mature placentas demonstrated robust GATA3 positivity. Both complete and partial Hydatidiform Moles (HMs) displayed widespread GATA3 expression in the cytotrophoblast and the trophoblast at the implantation site. Additionally, GATA3 expression exhibited variations in areas with extravillous trophoblast hyperplasia.[10]

Another study conducted by Dash SS et al. in 2022 focused on Epithelioid trophoblastic tumors (ETTs), which are extremely rare gestational trophoblastic tumors. They typically affect women of reproductive age, leading to abnormal vaginal bleeding and slightly elevated beta human chorionic gonadotrophin (B-hCG) levels. This report presents four cases of ETT in reproductive-age females, discussing their histomorphology, immunoprofiles, and diagnostic challenges. Patients had an average pre-treatment B-hCG level of 665.24 mIU/mL. Microscopically, ETTs displayed epithelioid characteristics with abundant eosinophilic cytoplasm, vesicular nuclei, and prominent nucleoli, often accompanied by hemorrhage, necrosis, and hyaline-like material. Immunohistochemical analysis consistently showed AE1/AE3 and p63 positivity in all cases, and GATA3 was positive in one case. Surgical intervention with hysterectomy was performed for all patients, and they had an average follow-up of 39.4 months, with a survival period averaging 32.8 months. All patients remained alive till the end of research duration.[11]

A case studied by Mannan R et al. in 2019 reported that Choriocarcinoma can manifest in unusual, extragenital sites like the lungs, mediastinum, retroperitoneum, or even the brain (referred to as nongestational choriocarcinoma). One exceptionally rare occurrence is choriocarcinoma developing in the urinary bladder, with only a handful of global cases reported. Identifying and providing a thorough diagnosis for this condition is crucial due to its poorer prognosis compared to conventional gestational choriocarcinoma. It necessitates more

aggressive chemotherapy. In this report, we present a case involving a 19-year-old girl with urinary bladder choriocarcinoma, highlighting the diagnostic challenges associated with it.[12]

GATA3 expression analysis can be valuable in autopsy and medicolegal investigations, particularly in cases related to illegal abortion and maternal deaths. In such cases, identifying fetal tissues in the maternal autopsy can be challenging. GATA3 expression can help confirm the presence of trophoblastic tissues, which are characteristic of pregnancy. Detecting GATA3 expression in these tissues can aid forensic pathologists in determining whether an abortion has taken place. By analyzing GATA3 expression in uterine tissues, forensic experts can help distinguish abortion-related maternal deaths from other causes. This information is crucial for accurate cause-of-death determination and legal investigations. GATA3 expression patterns can also provide insights into the stage of pregnancy at the time of abortion or maternal death. This feature gains importance in circumstances wherein gestational age could not be elicited by history or by previously existing records. This information can help investigators estimate gestational age, which is relevant in legal contexts including verification of abortion-related documents (if any) and can influence the charges in cases involving illegal abortions.GATA3 expression can aid forensic pathologists in confirming the presence of trophoblastic tissues, including villous trophoblasts, in the uterine specimens. Thus, GATA3 expression data can serve as valuable forensic evidence in legal proceedings. Information about GATA3 expression in cases of unsafe abortions can contribute to public health initiatives.[13,14] It helps in understanding the prevalence and consequences of unsafe abortions, which can inform policies and interventions aimed at reducing maternal mortality.

## 6.CONCLUSION

This study aimed to investigate GATA-3 expression in trophoblastic tissues and its potential in confirming uncertain histopathological diagnoses. The analysis revealed that nearly all cases (98.4%) expressed GATA3 in at least one type of trophoblast, with 20.4% expressing it in all three trophoblast types. Among specimens related to products of conception, GATA3 was consistently positive in intermediate trophoblast and cytotrophoblast tissues (100%), while syncytiotrophoblast tissue showed positive expression in only 20.4% of cases. In Hydatidiform mole specimens, GATA3 was positive in intermediate trophoblast and cytotrophoblast tissues (100%) but entirely negative in syncytiotrophoblast tissue. While GATA-3 was widely expressed, its utility in confirming uncertain histopathological diagnoses remains inconclusive based on this study's findings.



**Conflict Of Interest**: The authors declare no conflict of interest.

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## REFERENCES

1. Chou J, Provot S, Werb Z. GATA3 in development and cancer differentiation: cells GATA have it!. J. Cell. Physiol. 2010; 222; 42–49. doi: 10.1002/jcp.21943.
2. Zaidan N, Ottersbach K. The multi-faceted role of GATA3 in developmental haematopoiesis. Open Biology. 2018;8(11):180152. doi:10.1098/rsob.180152
3. Home P, Ray S, Dutta D et al. GATA3 is selectively expressed in the trophectoderm of peri-implantation embryo and directly regulates Cdx2 gene expression. J. Biol. Chem. 2009; 284; 28729–28737.DOI: 10.1074/jbc.M109.016840

4. Saben J, Zhong Y, McKelvey S et al. A comprehensive analysis of the human placenta transcriptome. Placenta 2014; 35; 125–131. doi: 10.1016/j.placenta.2013.11.007
5. Ralston A, Cox BJ, Nishioka N, Sasaki H, Chea E, Rugg-Gunn P, et al. GATA3 regulates trophoblast development downstream of tead4 and in parallel to CDX2. Development. 2010;137(3):395–403. doi:10.1242/dev.038828
6. Worldwide, an estimated 25 million unsafe abortions occur each year2017 [Internet]. World Health Organization; 2017 [cited 2023 August 24]. Available from: https://www.who.int/news/item/28-09-2017-worldwide-an-estimated-25-million-unsafe-abortions-occur-each-year#:~:text=Worldwide%2C%2025%20million%20unsafe%20abortions,Africa%2C%20Asia%20and%20Latin%20America.
7. Singh S et al., Abortion and Unintended Pregnancy in Six Indian States: Findings and Implications for Policies and Programs, New York: Guttmacher Institute, 2018. https://doi.org/10.1363/2018.30009
8. Bannet N, Gown AM, Shih M, Li QK, Roden RBS, Nucci MR et al. GATA-3 expression in trophoblastic tissues: An Immunohistochemical Study of 445 Cases, Including Diagnostic Utility. Am J Surg Pathol. 2015 January; 39(1): 101–8. doi:10.1097/PAS.0000000000000315.
9. Kumar V, Abbas A, Aster J. Robbins And Cotran Pathologic Basis Of Disease. 11th ed. Amsterdam, Netherlands: Elsevier publications; 2023.
10. Mirkovic J, Elias K, Drapkin R, Barletta JA, Quade B & Hirsch MS. GATA3 expression in gestational trophoblastic tissues and tumours. Histopathology 2015; 67: 636–44. DOI: 10.1111/his.12681
11. Dash SS, Sakhadeo U, Karmarkar S, Mittal N, Menon S, Rekhi B, et al. Epithelioid trophoblastic tumor: A case series. Indian J Pathol Microbiol 2023;66:148-51. Doi: 10.4103/ijpm.ijpm_212_22
12. Mannan R, Sharma S, Goyal S, Bhasin TS. Ectopic non-gestational pure choriocarcinoma of the urinary bladder in a young nulliparous female: A diagnostic challenge. Indian J Med Paediatr Oncol 2020;41:423-6. Doi: 10.4103/ijmpo.ijmpo_71_19
13. Grimes DA, Benson J, Singh S, et al.. Unsafe abortion: the preventable pandemic. The Lancet 2006;368:1908–19. Doi: 10.1016/S0140-6736(06)69481-6
14. Worldwide, an estimated 25 million unsafe abortions occur each year2017 [Internet]. World Health Organization; 2017 [cited 2023 August 24]. Available from: https://www.who.int/news/item/28-09-2017-worldwide-an-estimated-25-million-unsafe-abortions-occur-each-year#:~:text=Worldwide%2C%2025%20million%20unsafe%20abortions,Africa%2C%20Asia%20and%20Latin%20America.