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# Immature Teratoma and Teratoma Associated with Associated with Malignancies, Clinicopathological and Survival Outcome at AHPGIC

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## Abstract

**Aim:** To analyse the clinicopathogical features and the survival outcome of the nine cases of teratoma and immature teratoma associated with malignancies and immature teratoma alone.

**Material Methods:** The Case Included

1. HPS Confirmed Immature teratoma and teratoma with Malignancies After Staging Laparotomy

2. HPS Confirmed Cases of Immature Teratoma

Statistical Method of Analysis - Chi square test and Kaplan meyer survival analysis.

**Results**: The overall survival of immature teratoma is 66.7% with 95% confidence interval (.706, 1.000). The total survival in case of immature teratoma with associated is ther maignancies 66.7% with CI (.300, 1.000). In other hand the total survival in case of immature teratoma with other malignancies is 33.3% with CI (.0673, 1.000). This variability in the two groups of immature teratoma associated with malignancies is probably due two type of asscciated malignancies i.e embryonal and yolk sac and melanoma. The cases teratoma with squamos cell carcinoma all survived. Chi-square test on histology, shows there is no significant difference of survival pattern between different histology types at 5% level of significance. The total survival in case of low grade is 85.7% with CI (.633, 1.000). The total survival in case of high grade is 0.01%; which means there are very low survival in case of high-grade carcinoma. The total survival in case of Conservative surgery is 50% with CI (.225, 1.000); which means there are almost 50% survival in case of Conservative surgery. There is no death event happened in case of Radical surgery so survival cannot be estimated in such case. Thus, there is no significant difference of survival pattern between different treatment types at 5% level of significance (p= 0.2).

## Introduction

An immature teratoma is a teratoma that contains anaplastic immature elements, and is often synonymous with malignant teratoma [1] A teratoma is tumor of germ cell origin, containing tissues from more than one ge germ cell line2. An immature teratoma is very rare tumor, representing 1% of all teratomas, 1% of all ovarian cancer, and 35.6% of all malignant ovarian germ cell tumors. It displays aspecific age,of incidence its usual in first two decaded rare afer menopause.toma contains immature elements unlike mature teratoma , an immature elements

Totipotent neoplastic cells can differentiate along the embryonal or extraembryonal lines.

- The embryonal somatic differentation along a primitive embryonic cell lines results in embryonal carcinoma.\
- Extra embryonal differentiation along the trophoblastic line gives rise to choriocarcinoma.
- The yolk sac line give rise to yolk sac tumor (endodermal sinus tumor).

Immature teratoma in ultrasound appear nonspecific whereas at ct and mri predominantly solid with fat filled elements these patients of immature teratomaors are surgically staged via exploratory laparotomy with cytologic washings, peritoneal biopsies, an omental assessment (either biopsy or omentectomy) [3] laparoscopy is preferred mode in immature teratoma an immature teratoma contains varying compositions of adult and embryonic tissues. The most common component identified is the neuroectoderm [4].

Tumors may also present embryonic components such immature cartilageand skeletal muscleof mesodermal origin 5. Immature teratoma is composed of embronic endodermal derivatives [6].

Recently a reliable biomarker oct-4 are helpful in diagnosing malignant immature teratomas [7]

Thurlberg and schully devised a grading system on the basis of differentiation of the cellular element of the tumor The proportion of immature tissue elements defines the grade of maturity. This was later modified by Norris etal who added quantitative aspect to the the degree of immaturity.

Grade 1 and2 usually have a normal karyotype Wheras GRADE 3 has abnormal karyotype.But, there may be still Be detectable alterations in gene level Treatment depends on fertility and grade Since the occurrence of immature teratoma is rarely bilateral, current standard of care is unilateral salpingooopherectomy with sampling of peritoneal implants [9]. Total abdominal hysterectomy with bilateral salpingo-oopherectomy are not indicated as they do not influence the outcome [10].

Fertility sparing surgery is the form of treatment in young patients10.zhao etal reported that here is no significant differences in survival rates or post operative fertility outcomes between two.

### Aims and Objective of The Study

The aim of the study is to analyse the clinocopathological and survival outcome 10 cases of immature and mature teratoma associated with malignancies.

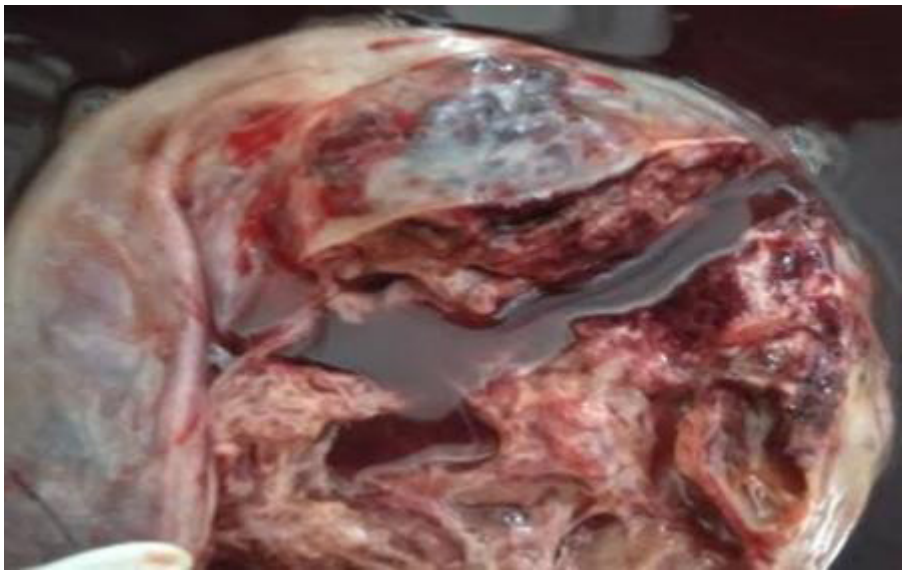
## Material Methods

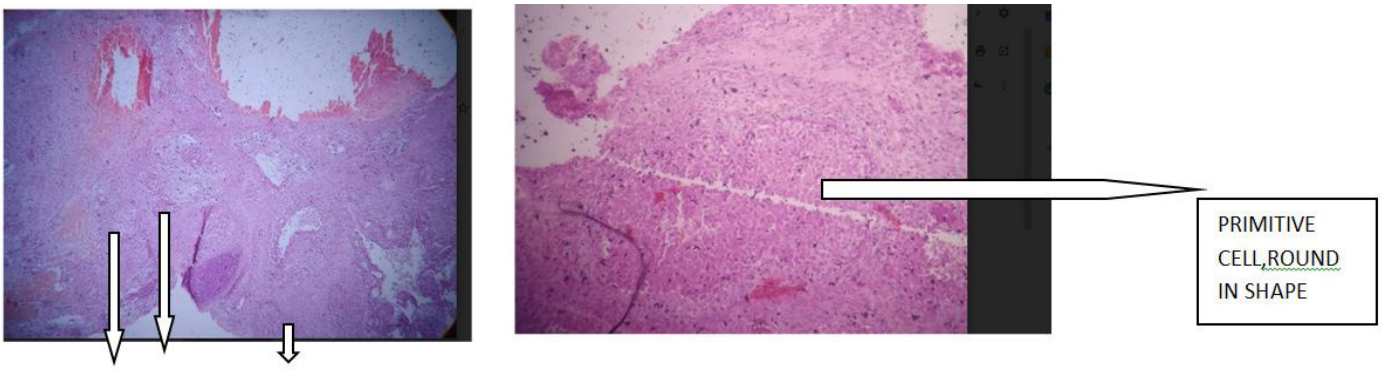
The case included-

1. HPS confirmed immature teratoma and teratoma and immature teratoma with malignancies after staging laparotomy.
2. HPS confirmed cases of teratoma.

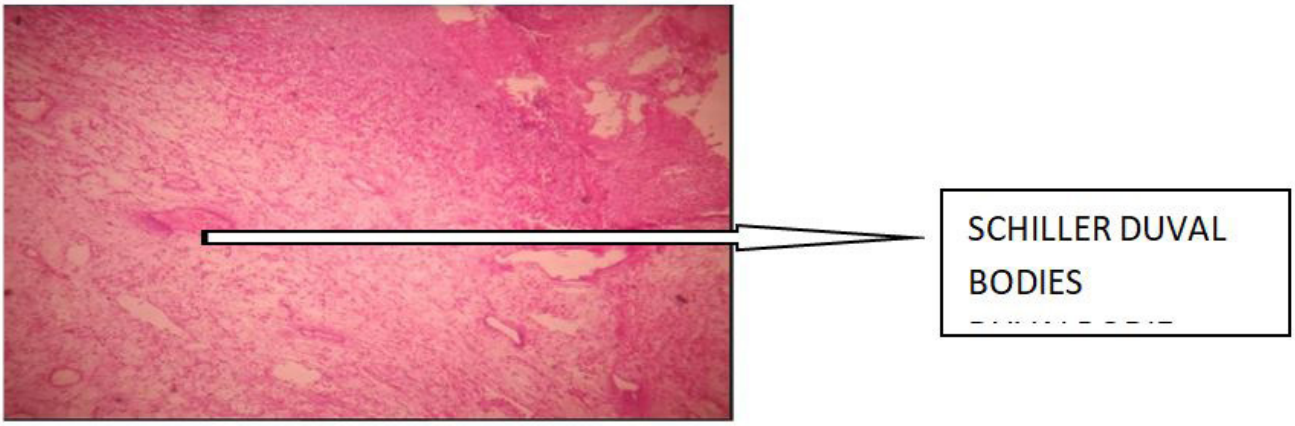
### Statistical Method of Analysis

Chi square test and Kaplan meyer survival analysis.





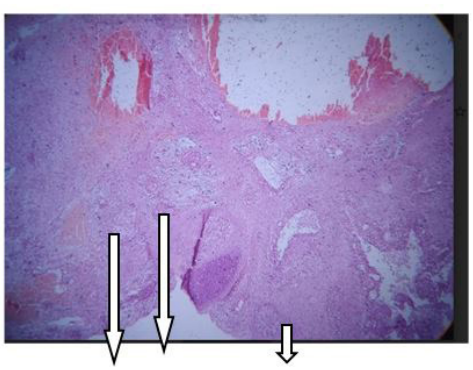

IMMATURE TERATOMA EMBRYONAL CARCINOMA WITH NEUROEPITHELIUM



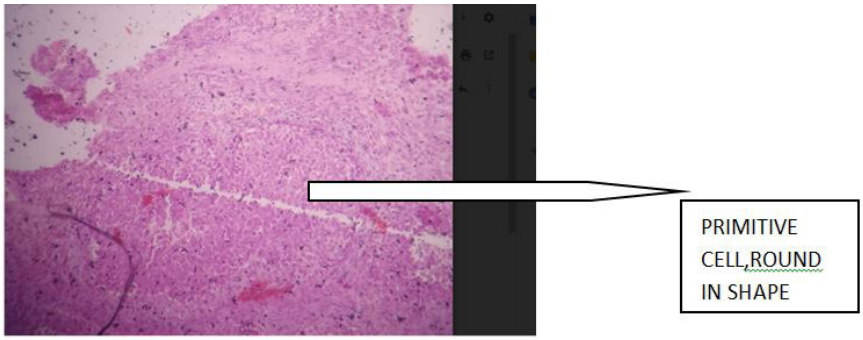

YOLK SAC COMPONENT

**Figure 1:** An Immature Teratoma with Neuroepithelium, Yolksac and Embronal Carcinoma

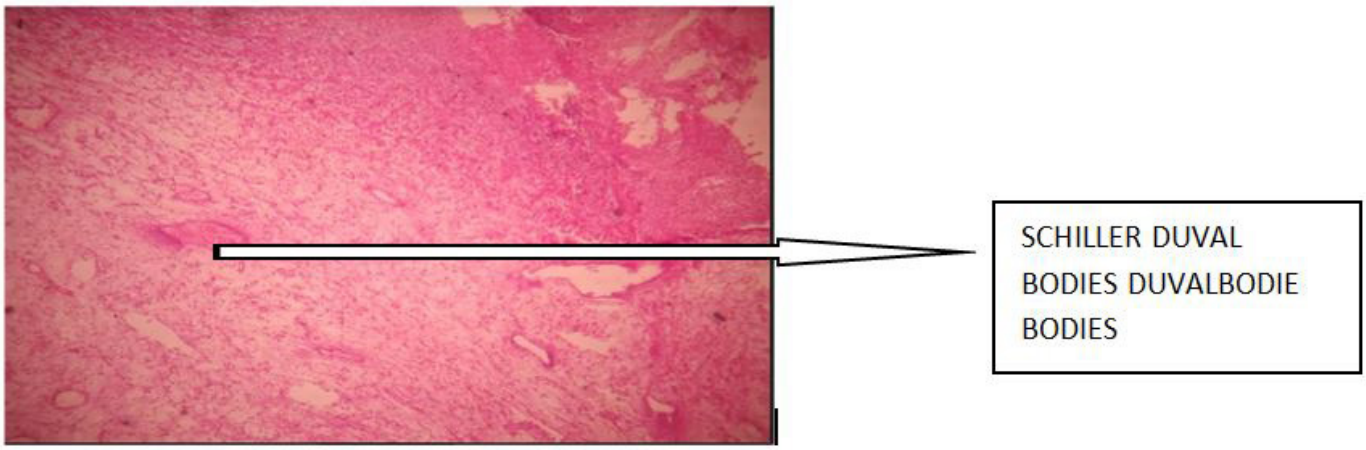
**Descriptive Statistics** – Total no of cases takenfor analysis is 10. immature teratoma alone3(30%),immatureteratoma with malignancies 3(30%) and teratoma with malignancies 4(40%). Table1immature teratma asocited with malignancies were one with yolk sac component, one with melanoma and one with embryonal carcinoma



IMMATURE TERATOMA




EMBRYONAL CARCINOMA WITH NEUROEPITHELIUM




YOLK SAC COMPONENT

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | immature teratoma | 3 | 30.0 | 30.0 | 30.0 |
| | immature teratoma with other malignancies | 3 | 30.0 | 30.0 | 60.0 |
| | teratoma with squamous cell carcinoma | 4 | 40.0 | 40.0 | 100.0 |
| | Total | 10 | 100.0 | 100.0 | |

Age and followup interval Table 2

| | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| age | 10 | 12.00 | 60.00 | 34.7000 | 17.08833 |
| Follow up time (in months) | 10 | 12.00 | 60.00 | 46.8000 | 18.28661 |
| Valid N (listwise) | 10 | | | | |

An Immature Teratoma with Neuroepithelium, Yolksac and Embronal Carcinoma

The median age is 34 years with a minimum twelve and maximum 60 years Table 2. The follow up was a upto 60 months, minimum was 12 months. allthe the three cases f malignancies were followed up.

The case with a endodermal component presented the second year and the one with embryonal component in the 3rd year and the one with melanomain the first year.

The markers considered were ldh, bhcg,. Ldh was >400IU in 8(80%) and less <400IU in 2(20%) table 3.beta HC-G<1Miu in 3(30%), beta hcg>1Miu(70%) table 4. The low grade

7 (70%) cases and high grade 3(30%) table 5The treatment was basically two groups. Conservative surgery group i.e unilateral-salpingoopherectomy7(70%), radical surgery group i.e b/l salpingooopherectomy 3(30%) table 6. There were 8 (80%) in stage 1a and one in stageIII (10%)table7 and one in stage 1c2(10%). The cases of immature teratma associated with ther malignancies i.e embryonal, yolk sac cmpnent and melanoma received adjuvant ct 6 cycles. Whereas the four teratoma with squamous cell carcinomas and those with immature teratomas alone i.e 4 cases without adjuvant were followed up.

The case with immature teratma associated with embryonal carcinoma presented in stageIII, The ther two cases of immature teratoma associated with endormal sinus and that with maelanma presented instage ic2 and stage1a respectively. The four cases teratoma with squamos cell carcinoma presented in stage 1a.and the three cases imaature teratoma alne presented in stage 1a

| | | Frequency | Percent | Valid Percent | Cumulative Percent | |
|---|---|---|---|---|---|---|
| Valid | <400 | 2 | 20.0 | 20.0 | 20.0 | 20.0 |
| | >400 | 8 | 80.0 | 80.0 | 100.0 | |
| | Total | 10 | 100.0 | 100.0 | | |

**Table 3-LDH**

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | <1 | 3 | 30.0 | 30.0 | 30.0 |
| | >1 | 7 | 70.0 | 70.0 | 100.0 |
| | Total | 10 | 100.0 | 100.0 | |

**Table 4- BETA_HCG**

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | Low | 7 | 70.0 | 70.0 | 70.0 |
| | High | 3 | 30.0 | 30.0 | 100.0 |
| | Total | 10 | 100.0 | 100.0 | |

**Table 5:** All the three cases of immature teratma with malignancies presented in higher grade.The other cases of immature teratoma and teratma associated with squamous cell carcinoma presented in lower grade

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | Conservative surgery | 6 | 60.0 | 60.0 | 60.0 |
| | radical surgery | 4 | 40.0 | 40.0 | 100.0 |
| | Total | 10 | 100.0 | 100.0 | |

**Treatment Table 6**

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | stage 1a | 8 | 80.0 | 80.0 | 80.0 |
| | stage III | 1 | 10.0 | 10.0 | 90.0 |
| | stage1c2 | 1 | 10.0 | 10.0 | 100.0 |
| | Total | 10 | 100.0 | 100.0 | |

**Stage Table 7**

**Treatment * Histology Crosstabulation**

| | | Histology | | | Total |
|---|---|---|---|---|---|
| | | immature teratoma | immature teratoma with other malignancies | teratoma with squamous cell carcinoma | |
| treatment | Conservative surgery | 3 | 3 | 0 | 6 |
| | radical surgery | 0 | 0 | 4 | 4 |
| Total | | 3 | 3 | 4 | 10 |

**Table 8- Count**

**Chi-Square Tests**

| | Value | df | P- value |
|---|---|---|---|
| Pearson Chi-Square | 10.000[a] | 2 | .007 |
| Likelihood Ratio | 13.460 | 2 | .001 |
| N of Valid Cases | 10 | | |

a. 6 cells (100.0%) have expected count less than 5. The minimum expected count is 1.20.

**Grade * Histology Crosstabulation**

| | | Histology | | | Total |
|---|---|---|---|---|---|
| | | immature teratoma | immature teratoma with other malignancies | teratoma with squamous cell carcinoma | |
| Grade | Low | 3 | 1 | 3 | 7 |
| | High | 0 | 2 | 1 | 3 |
| Total | | 3 | 3 | 4 | 10 |

**Table 9- Count**

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 3.254[a] | 2 | .197 |
| Likelihood Ratio | 3.900 | 2 | .142 |
| N of Valid Cases | 10 | | |

a. 6 cells (100.0%) have expected count less than 5. The minimum expected count is .90.

**stage * Histology Crosstabulation**

| | | Histology | | | Total |
|---|---|---|---|---|---|
| | | immature teratoma | immature teratoma with other malignancies | teratoma with squamous cell carcinoma | |
| Stage | stage 1a | 2 | 2 | 4 | 8 |
| | stage III | 0 | 1 | 0 | 1 |
| | stage1c2 | 1 | 0 | 0 | 1 |
| Total | | 3 | 3 | 4 | 10 |

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 5.000[a] | 4 | .287 |
| Likelihood Ratio | 5.142 | 4 | .273 |
| N of Valid Cases | 10 | | |

a. 9 cells (100.0%) have expected count less than 5. The minimum expected count is .30.

**LDH * Histology Crosstabulation**

| | | Histology | | | Total |
|---|---|---|---|---|---|
| | | immature teratoma | immature teratoma with other malignancies | teratoma with squamous cell carcinoma | |
| LDH | <400 | 1 | 0 | 1 | 2 |
| | >400 | 2 | 3 | 3 | 8 |
| Total | | 3 | 3 | 4 | 10 |

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 1.146[a] | 2 | .564 |
| Likelihood Ratio | 1.690 | 2 | .429 |
| N of Valid Cases | 10 | | |

a. 6 cells (100.0%) have expected count less than 5. The minimum expected count is .60.

**BETA_HCG * Histology Crosstabulation**

| | | Histology | | | Total |
|---|---|---|---|---|---|
| | | immature teratoma | immature teratoma with other malignancies | teratoma with squamous cell carcinoma | |
| BETA_HCG | <1 | 2 | 1 | 0 | 3 |
| | >1 | 1 | 2 | 4 | 7 |
| Total | | 3 | 3 | 4 | 10 |

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 3.651[a] | 2 | .161 |
| Likelihood Ratio | 4.579 | 2 | .101 |
| N of Valid Cases | 10 | | |

a. 6 cells (100.0%) have expected count less than 5. The minimum expected count is .90.

**Status * Histology Crosstabulation**

| | | Histology | | | Total |
|---|---|---|---|---|---|
| | | immature teratoma | immature teratoma with other malignancies | teratoma with squamous cell carcinoma | |
| Status | Survive | 2 | 1 | 4 | 7 |
| | Death | 1 | 2 | 0 | 3 |
| Total | | 3 | 3 | 4 | 10 |

**Chi-Square Tests**

| | Value | df | Asymp. Sig. (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 3.651[a] | 2 | .161 |
| Likelihood Ratio | 4.579 | 2 | .101 |
| N of Valid Cases | 10 | | |

**Table 13 :** a. 6 cells (100.0%) have expected count less than 5. The minimum expected count is .90.

Cross tabulation analysis done of the individual factors i.e grade, stage, markers (ldh.bhcg),type of surgery ,with histology using the pearson chiquare and likehod ratio. Each factor analysed with three histolgical groups i.e immature teratma, immature teratoma with malignanciesand teratoma with malignancies the only significant assciation was that f type f suregery with the three grups with a p value-.007.

**Survival analysis**

**Overall Survival Analysis**

| time | n.risk | n.event | survival | std.err | lower 95% CI | upper 95% CI |
|---|---|---|---|---|---|---|
| 24 | 9 | 1 | 0.889 | 0.105 | 0.706 | 1 |
| 36 | 8 | 2 | 0.667 | 0.157 | 0.420 | 1 |

Here it can be observed that the overall survival is 66.7% with 95% confidence interval (.706, 1.000)

**Overal Survival Plot**

**Table 14**

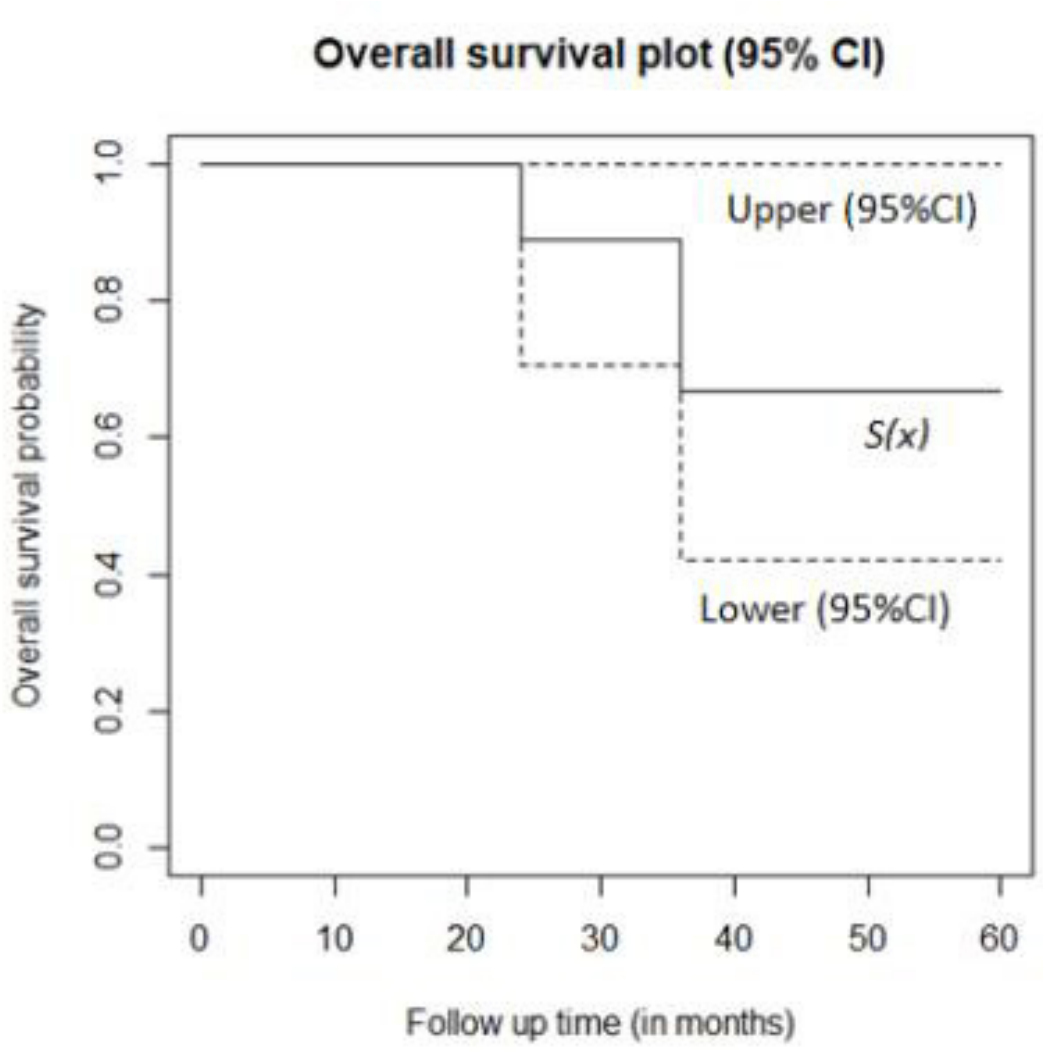



**Figure 2:** Over all aurvival Probability

**Descriptive Statistics (Histology)**

| Histology | n | events | median | 0.95LCL | 0.95UCL |
|---|---|---|---|---|---|
| immature teratoma | 3 | 1 | NA | 36 | NA |
| immature teratoma with other malignancies | 3 | 2 | 36 | 24 | NA |
| teratoma with squamous cell carcinoma | 4 | 0 | NA | NA | NA |

**Table 15**

**HistologyThree category Survival Analysis**

| Histology Type | Time (in months) | n.risk | n.event | survival | std.err | lower 95% CI | upper 95% CI |
|---|---|---|---|---|---|---|---|
| immature teratoma | 36 | 3 | 1 | 0.667 | 0.272 | 0.300 | 1.000 |
| immature teratoma with other malignancies | 24 | 3 | 1 | 0.667 | 0.272 | 0.2995 | 1.000 |
| | 36 | 2 | 1 | 0.333 | 0.272 | 0.0673 | 1.000 |
| teratoma with squamous cell carcinoma | NA | NA | NA | NA | NA | NA | NA |

The total survival in case of immature teratoma is 66.7% with CI (.300, 1.000). In other hand the total survival in case of immature teratoma with other malignancies is 33.3% with CI (.0673, 1.000)

Overall survival of immature teratoma is 66.7% with 95% confidence interval (.706, 1.000). The immature teratoma assciated with malignancies are divided into two categories the total survival in case of immature teratoma with associated is ther maignancies 66.7% with CI (.300, 1.000) total survival in case of immature teratoma with other malignancies is 33.3% with CI (.0673, 1.000). The cases teratoma associated with squamous cell carcinoma had no disease recurrence and all the 4 cases had survived

**HistologyThree category Survival Plot**

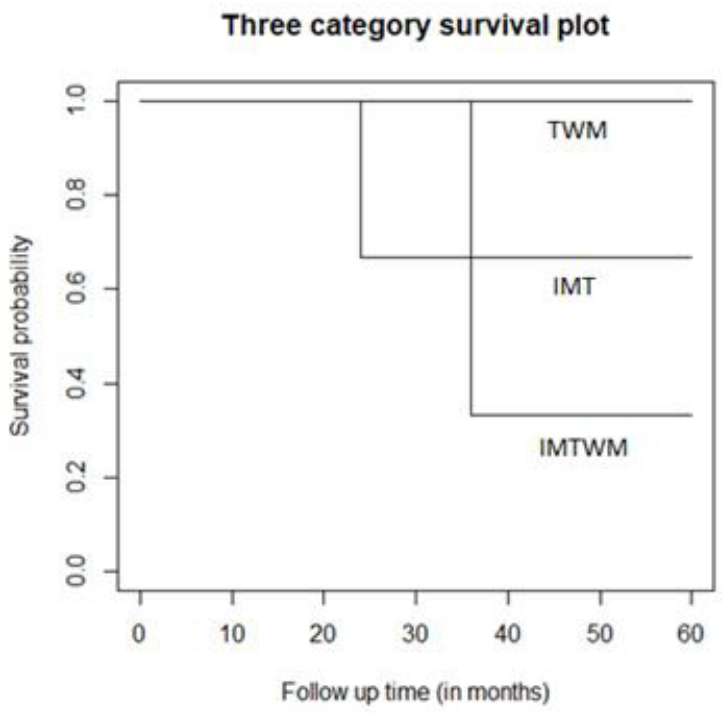
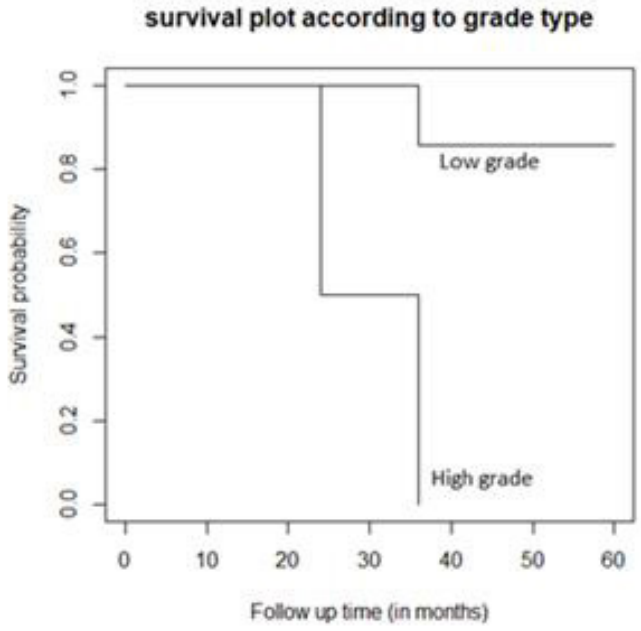



**Figure 3:** Overall survival analysis of the three groups i.e immature teratoma(imt), teratoma with bmalignancies(twm), immature teratoma with malignancies(imtwm)

**Grade (two category) Survival Plot**




From the above plot it can be said there are high survival in case of low grade and low survival in case of high grade.

**Figure 4:** Grade Survival Plot

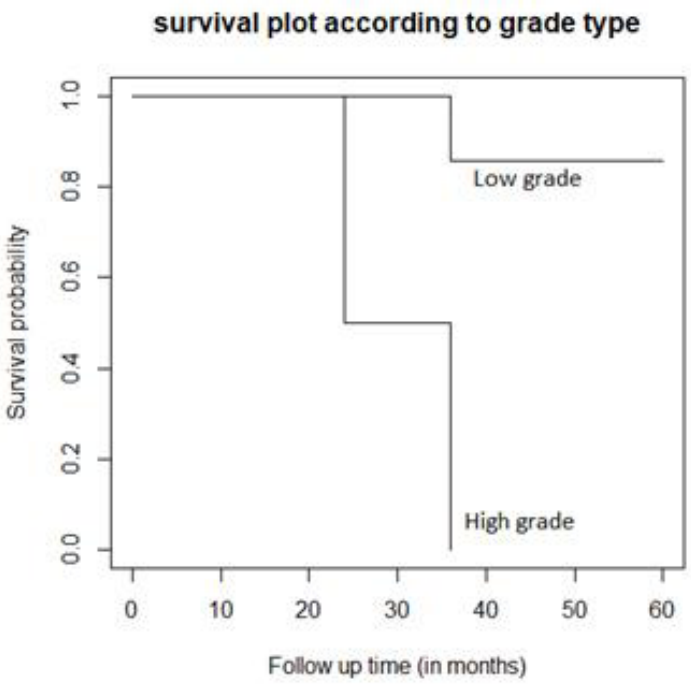
**Chi-square test on Grade**

| grade | N | Observed (O) | Expected (E) | (O-E)^2/E | (O-E)^2/V |
|---|---|---|---|---|---|
| Low | 7 | 1 | 2.528 | 0.923 | 6.48 |
| High | 3 | 2 | 0.472 | 4.943 | 6.48 |

N.B.: Chisq= 6.5 on 1 degrees of freedom, p= 0.01

**Table 17**

## Grade (two category) Survival Plot




From the above plot it can be said there are high survival in case of low grade and low survival in case of high grade.

**Chi-square test on Grade**

| grade | N | Observed (O) | Expected (E) | (O-E)^2/E | (O-E)^2/V |
|---|---|---|---|---|---|
| Low | 7 | 1 | 2.528 | 0.923 | 6.48 |
| High | 3 | 2 | 0.472 | 4.943 | 6.48 |

N.B.: Chisq= 6.5 on 1 degrees of freedom, p= 0.01

**DescriptiveStatistics (Treatment)**

| Treatment | n | events | median | 0.95LCL | 0.95UCL |
|---|---|---|---|---|---|
| Conservative surgery | 6 | 3 | 36 | 36 | NA |
| Radical surgery | 4 | 0 | NA | NA | NA |

Among total 10 cases, there are 6 cases with Conservative surgeryand 4 cases with Radical surgery. 3 deaths can be observed in the Conservative surgerycategory where as in Radical surgery there is no death case.

**Treatment(Two category) Survival Analysis**

| Treatment | Time (in months) | n.risk | n.event | survival | std.err | lower 95% CI | upper 95% CI |
|---|---|---|---|---|---|---|---|
| Conservative surgery | 24 | 6 | 1 | 0.833 | 0.152 | 0.583 | 1.000 |
| | 36 | 5 | 2 | 0.500 | 0.204 | 0.225 | 1.000 |
| Radical surgery | NA | NA | NA | NA | NA | NA | NA |

The total survival in case of Conservative surgeryis 50% with CI (.225, 1.000); which means there are almost 50% survival in case of Conservative surgery. There is no death event happened in case of Radical surgery so survival cannot be estimated in such .case

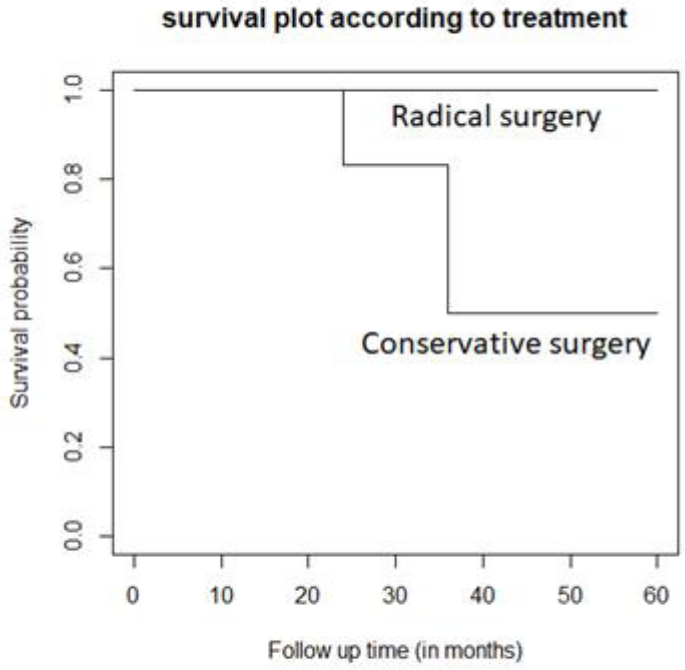
**Chi-square test on Treatment**

| Treatment | N | Observed (O) | Expected (E) | (O-E)^2/E | (O-E)^2/V |
|---|---|---|---|---|---|
| Conservative Sugery | 6 | 3 | 1.92 | 0.612 | 1.88 |
| Radical Surgery | 4 | 0 | 1.08 | 1.083 | 1.88 |

N.B.: Chisq= 1.9 on 1 degrees of freedom, p= 0.2

Thus, there is no significant difference of survival pattern between different treatment types at 5% level of significance (p= 0.2).

**Treatment (two category) Survival Plot**




From the above plot it can be said there are high survival in case of Radical surgery and low survival in case of Conservative surgery.

## Results

Here it can be observed that the overall survival of immature teratoma is 66.7% with 95% confidence interval (.706, 1.000). The total survival in case of immature teratoma with associated is ther maignancies 66.7% with CI (.300, 1.000). In other hand the total survival in case of immature teratoma with other malignancies is 33.3% with CI (.0673, 1.000). this variability in the two groups of immature teratoma associated with malignancies is probably due two type of asscciated malignancies i.e embryonal and yolk sac and melanoma. The cases teratoma with squamos cell carcinoma all survived. Chi-square test on histology, shows there is no significant difference of survival pattern between different histology types at 5% level of significance. Among total 10 cases, there are 7 cases with low grade and 3 cases with high grade carcinoma. One death can be observed in the low-grade category where as in high grade category there are 2 death cases. The total survival in case of low grade is 85.7% with CI (.633, 1.000). The total survival in case of high grade is 0.01%; which means there are very low survival in case of high grade carcinoma. Among total 10 cases, there are 6 cases with Conservative surgery and 4 cases with Radical surgery. 3 deaths can be observed in the Conservative surgery category where as in Radical surgery there is no death case. The total survival in case of Conservative surgery is 50% with CI (.225, 1.000); which means there are almost 50% survival in case of Conservative surgery. There is no death event happened in case of Radical surgery so survival cannot be estimated in such case. From the above survival plot it can be said there are high survival in case of Radical surgery and low survival in case of Conservative surgery.Thus, there is no significant difference of survival pattern between different treatment types at 5% level of significance (p= 0.2).

## Conclusion

The median age of presentation was 34 yrs although the lowest age being 12yrs to uppermst age 60 yrs. Maximum nos case of immature teratoma were low grade and early stage. The immature teratma associated with malignancies were higher grade.The The conservative approach was preferred in early stage and low grade .The overall survival of immature teratoma is better than overall survival of immature teratoma with malignancies. The type of

associated malignancies i.e yolk sac and embryonal cmponent can differently affect the survival. Teratoma with squamous cell carcinoma has a good survival in early stage The low-grade type has better survival. The radical surgery group shows a better outcome.

The rarity of such cases, and early age of presentation prompted us to analyse there clinicopathlogical and survival factors. So, that it could be of help to others in deciding the radicality of management on the basis of the above factors.

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