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## CONTENTS OF THE ISSUE

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- i. Copyright Notice
- ii. Editorial Board Members
- iii. Chief Author and Dean
- iv. Contents of the Issue
  
- 1. Correlation of Maternal Age and Chromosomal Abnormality in Products of Conception- A Single Centric Study. **1-5**
- 2. Association of Thyroid Autoimmunity and Thyroid Dysfunction in Women with Infertility. **7-11**
- 3. Analysis of Cesarean Section Rate using Robson 10 Group Classification System in a Tertiary Hospital: An Observational Study. **13-18**
- 4. Uterine Leiomyosarcoma in a Young Unmarried Lady- A Case Report. **19-21**
  
- v. Fellows
- vi. Auxiliary Memberships
- vii. Preferred Author Guidelines
- viii. Index





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## Correlation of Maternal Age and Chromosomal Abnormality in Products of Conception- A Single Centric Study

By Dr. Yamini Jadhav, Vidya Bhairi, Ajinkya Jadhav, Bhagyashree Gedam, Vedant Patole, Shweta Parab & Dr. Jayaram Kandandale

**Abstract- Purpose:** The purpose of this study is to find out the types and incidence rate of chromosomal abnormalities and the relationship between maternal age and chromosomal abnormality in products of conception by retrospective analysis.

**Method:** Karyotype study using standard GTG banding and FISH study for aneuploidy detection was done from products of conception samples.

**Results:** A total of 513 cases of products of conception were studied retrospectively. 98 cases were studied by conventional cytogenetic technique and 415 cases were studied by a FISH method. The chromosomal abnormality was observed in 97 cases (18.91%). Trisomy was found to be a major chromosomal abnormality amongst the cases studied, followed by triploidy and monosomy. A higher incidence of chromosomal abnormality was found in women with advanced maternal age as compared to the maternal age less than 35 years.

**Keywords:** karyotype, products of conception, FISH, chromosome abnormality, maternal age.

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# Correlation of Maternal Age and Chromosomal Abnormality in Products of Conception- A Single Centric Study

Dr. Yamini Jadhav <sup>α</sup>, Vidya Bhairi <sup>σ</sup>, Ajinkya Jadhav <sup>ρ</sup>, Bhagyashree Gedam <sup>ω</sup>, Vedant Patole <sup>¥</sup>, Shweta Parab <sup>§</sup> & Dr. Jayaram Kandandale <sup>x</sup>

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**Conclusions:** Pregnancy loss is high in women with advanced maternal age group. The study of products of conception helps the couple to recognize the cause of miscarriage. These results help the couple to cope up with the emotional burden of miscarriage and in the future pregnancy management.

**Keywords:** karyotype, products of conception, FISH, chromosome abnormality, maternal age.

## I. INTRODUCTION

Advanced maternal age is defined as a pregnancy in women at 35 years of age or more regardless of parity, whether the conception is first or not. Reproductive health is a state of complete mental, physical, and social well-being related to all stages of reproductive processes [1]. Delayed motherhood due to carrier opportunities and changes in marriage pattern, use of contraception, social support, and other possible factors such as stress, pollutants, and smoking habits are responsible for the increase in the rate of pregnancy loss or miscarriage. The trend of delaying pregnancy has been observed worldwide.

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Miscarriage is one of the most recognizable difficulties during pregnancy. The rate of miscarriage in known pregnancies is 15-20% [2]. Most pregnancy losses occurred during the first trimester. The frequency of pregnancy loss due to the presence of aneuploidy or unbalance chromosomal abnormality is about 50-60% [2-4].

Fetal chromosomal abnormalities may result due to abnormal gametogenesis during the process of fertilization or during the first cellular division of the zygote. Many pregnancies fail in the early-stage and hence may not be clinically recognized. Approximately 30% of pregnancies end with live birth. After three pregnancy failures, the risk of miscarriages increases to 35% [5].

It is necessary to carry out laboratory testing of the products of conception to help to recognize the cause of miscarriage. These results help the couple to cope up with the emotional burden of miscarriage and in the future pregnancy management [6, 7].

A systematic study of abnormalities detected in products of conception (POC) is necessary; hence we present here the results of karyotype and FISH studies of POC specimens and studied the effect of maternal age on pregnancy loss. With this study, we hope to provide updated and add-on perspective to the current knowledge of chromosomal abnormalities.

## II. MATERIAL AND METHODS

### a) Study Specimens

The retrospective study was performed on the products of conception samples received at the clinical cytogenetics department. Proper collection and transport guidelines for POC sample collection are circulated and explained to the centers sending the samples. For all first-trimester pregnancy losses, the abortus material was collected in a sterile container with transport media under aseptic precautions.

The results were archived from the laboratory database, and in addition to maternal age, no personal information from the patients was included. As the laboratory receives material from different medical facilities with limited information, clinical data such as gestational age at the time of abortion and clinical

history of the parents were not available for all the samples received. A total of 513 results from POC analysis were performed.

Our study has been performed in two groups. Group I consists of cases with maternal age 18 to 34 years, and Group II consists of cases with advanced maternal age group (Age 35 years and above).

#### b) Cytogenetic and FISH analysis

All the POC specimens received were cleaned to remove decidual tissues as well as bloodstains. Then the tissue samples were digested using trypsin and collagenase. After tissue digestion, it was divided for the culture set up for karyotype and the FISH study. The karyotype, as well as FISH, was done using the standard protocol. The FISH study was performed for

aneuploidy detection which includes chromosomes 13, 18, 21 and sex chromosomes. For each probe mix, 50 interphase cells were studied.

The GTG banding was done for the karyotype study, and for each case a minimum of 20 metaphases was analyzed. Karyotype nomenclature was designated as per an international system for human cytogenomic nomenclature (ISCN 2016) [8].

### III. RESULTS

Out of 513 cases 416 cases showed normal results for Group I and II and 97 cases showed chromosomal abnormalities (Table 1). The rate of abnormality in the overall study was 18.91 % (97/513).

Table 1: Distribution of studied cases

	n	Age Group	
		18-34 Years	35 Years and above
<b>NORMAL</b>	416	361 (83%)	55 (71%)
<b>ABNORMAL</b>	97	75 (17%)	22 (29%)
<b>TOTAL</b>	513	436	77

Out of the 97 abnormal cases trisomy was seen in 45.36% (n=44) cases followed by monosomy and triploidy in 25.77% (n=25) and 27.84% (n=27) each.

Monosomy X was seen in 23.71% of cases followed by Trisomy 18 in 18.56%, Trisomy 21 in 13.4% and Trisomy 13 in 9.28% cases (Table 2).

Table 2: Distribution of chromosomal abnormality based on age group

Chromosome anomaly	Age Group		Total Abnormal Cases (%)
	18-34 Years	35 Years and above	
Trisomy 6	1	0	1 (1.03%)
Trisomy 7	0	1	1 (1.03%)
Trisomy 10	0	1	1 (1.03%)
Trisomy 13*	7	2	9 (9.28%)
Trisomy 16	1	0	1 (1.03%)
Trisomy 18	12	6	18 (18.56%)
Trisomy 21**	8	5	13 (13.40%)
Monosomy X	20	3	23 (23.71%)
Monosomy 18	1	0	1 (1.03%)
Monosomy 21	0	1	1 (1.03%)
Triploidy	24	3	27 (27.84%)
Tetraploidy	1	0	1 (1.03%)
<b>Total</b>	<b>75</b>	<b>22</b>	<b>97</b>

\*46, der(15)t(13;15)(q10;q10), +13 and 46,t(8;12), rob(13;14), +13 were counted in Trisomy 13 group.

\*\*46, der(14;21)(q10;q10), +21 was counted in Trisomy 21 group.

In terms of abnormality, we found that, the highest frequency was Trisomy followed by Monosomy X and Trisomy 18.

In the age group below 35 years, 83% had normal results, whereas abnormalities were found in 17% of cases. For the advanced maternal age group

(Age 35 years and above), normal results were found in 71% of cases and abnormal results in 29% of cases. The rates of abnormal results were significantly higher for the advanced maternal age group when compared to the younger maternal age group (Figure 1).

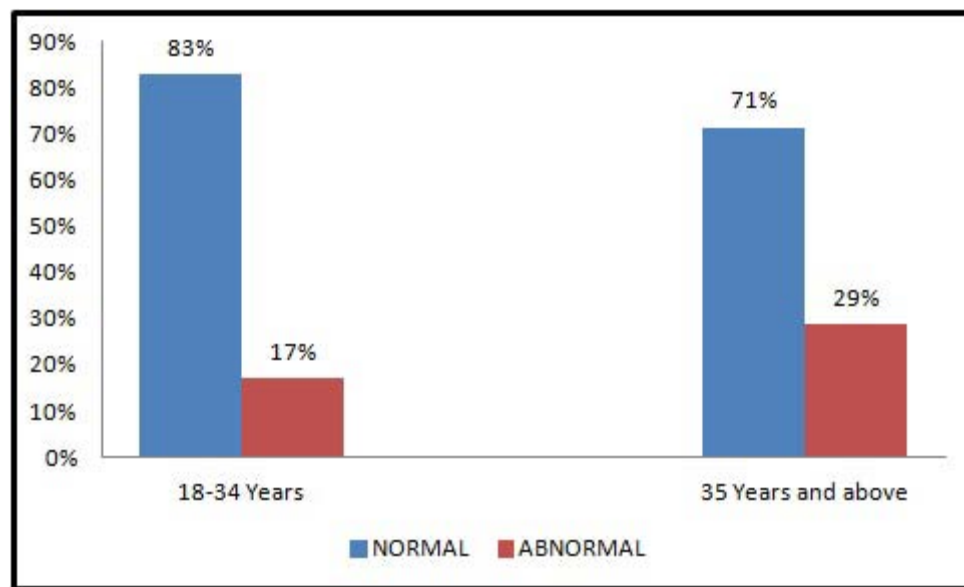


Figure 1: The relationship between maternal age and chromosomal abnormality.

#### IV. DISCUSSION

The etiology of pregnancy loss is heterogeneous which involves association among maternal, paternal and placental or fetal risk factors in pathways associated with conception and, fetal growth. The maternal risk factor includes infection, endocrine, anatomic, immunological and genetic abnormalities whereas embryonic defects such as chromosomal abnormality reduces embryonic development. The rate of miscarriage is higher after the age of 30 -35 years due to declined potential fertility.

For couples with a history of recurrent miscarriages, it is ideal to study the POC specimen where couples karyotype study shows normal karyotype results. Hence to know the genetic etiology behind the pregnancy loss and it is recommended to study POC specimen, where fetal chromosomal abnormality can be ruled out (if any).

Different types of chromosomal abnormalities are linked with different clinical states. The occurrence of trisomy increases with increasing maternal age, which is due to the meiotic non-disjunction that occurred during gametogenesis. In the present study, the most frequent trisomy type is trisomy 18, followed by trisomy 21 and trisomy 13. Aneuploidies account for the largest amongst the abnormalities detected in POC, same as Menasha et al. [3].

The most commonly observed chromosomal abnormality is Trisomy followed by triploidy which is resulted due to abnormal fertilization. The presence of autosomal monosomy is very rare in pregnancy loss. In the present study we have found one case with monosomy 21 and monosomy 18 each. Monosomy X is most frequently observed amongst pregnancy losses. Twenty-three cases of monosomy X were found in our

study. The structural abnormalities found in pregnancy loss are mainly translocations and inversions. In our study, the structural abnormalities were observed in 3 cases along with trisomy. One case of trisomy 21 along with translocation involving chromosome 14 and 21, karyotype result: 46, der(14;21)(q10;q10),+21. One case of trisomy 13 along with translocation involving chromosome 13 and 15, karyotype result: 46, der(15)t(13;15)(q10;q10),+13 and one case of trisomy 13 along with double translocation, karyotype result: 46, t(8;12), rob(13;14),+13 was seen in the study.

Presence of chromosomal abnormality in one of the parents results in a structural abnormality in the fetus. About 2-5% of couples with translocations experience repeated pregnancy losses [9-12].

The frequency of translocation amongst the couples with recurrent pregnancy losses is 40% for Robertsonian translocation and 60% for reciprocal translocations [13]. As compared to male partners, the balance chromosomal abnormalities are found twice in female partners. This is due to the fact that, the chromosomal abnormalities that are compatible with female fertility may result in male sterility.

In our study we have found higher abnormality rate (29%) in advanced maternal age group as compare to younger population studied (17%). The present findings consistent with the studies that reported the increased incidence of chromosomal abnormality with increasing maternal age [14-16]. Various studies have concluded that the women's with advanced maternal age have a higher incidence of unfavourable reproductive outcomes such as complications during pregnancy, spontaneous pregnancy loss, infertility or congenital anomalies in foetus as compared to the younger women which is consistent with the present study [17-22].

Study of products of conception using karyotype technique is highly suggested as it studies structural as well as numerical abnormalities. It has some drawback such as longer time, for reporting, laborious processing, and culture failure. Since we receive products of conception samples from various locations for testing, the FISH method plays an important role for aneuploidy detection of chromosome 13, 18, 21, X and Y. Advances in new techniques, help to improve the detection of abnormalities and subsequently increases the diagnostic abilities. The use of interphase FISH has allowed cytogenetic setups to study POC samples that have failed to grow hence failed to report the results.

## V. CONCLUSION

Pregnancy loss is high in women with advanced maternal age group and should be taken into consideration during pregnancy planning. Irrespective of previous pregnancy outcomes, maternal age at the time of conception is an independent and strong risk factor for fetal demise.

For the cost-effective management of the couple with a history of recurrent pregnancy losses, genetic evaluation for chromosomal abnormalities, if any, in POC samples plays an important role in avoiding the expensive non-genetic work up and also to understand the etiology behind pregnancy losses.

Genetic counseling is important in the clinical management of pregnancy losses to identify the recurrent risk in future pregnancy influenced by karyotype results. Hence finding this information in an accurate, fast and, reliable manner is critical. Other molecular testing methods such as array CGH and sequencing are useful in the detection of numerical aberrations such as monosomy or trisomy. Structural chromosomal aberrations, tetraploidy, polymorphism may be difficult to identify depending on the method used for detection. Hence the possible algorithm for assessing products of conception could be conventional karyotype study followed by FISH testing, which can identify the common trisomy, tetrasomy, or polyploidy.

New technologies such as Microarray, NGS studies of POC are still not commonly used due to high cost, the difficulty of CNV interpretation, inability to detect balanced chromosomal translocation, and limitation of ploidy change detection in some microarray platforms. However, both these techniques enable fast genetic testing and atomization; we believe that these testing will be implemented in wide practice soon.

The limitation of present study is small sample size and unavailability of maternal cell contamination data hence, further study is necessary to address these problems.

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### Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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# Association of Thyroid Autoimmunity and Thyroid Dysfunction in Women with Infertility

By Dorothy Shahnaz Mukul Fatema, Abdul Khaleque & Pratima Rani Biswas

*Patuakhali Medical College*

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**Objective:** The study aims to determine the association of thyroid autoimmunity (antithyroglobulin and antithyroid peroxidase) and thyroid dysfunction (hypo-or hyperthyroidism) among women with infertility.

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**Keywords:** *thyroid autoimmunity, thyroid dysfunction, infertility.*

**GJMR-E Classification:** NLMC Code: WK 200



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# Association of Thyroid Autoimmunity and Thyroid Dysfunction in Women with Infertility

Dorothy Shahnaz Mukul Fatema <sup>α</sup>, Abdul Khaleque <sup>σ</sup> & Pratima Rani Biswas <sup>ρ</sup>

**Abstract- Background:** In women of reproductive age, thyroid illness is the second most frequent endocrine disorder. While overt thyroid disease is well known as a cause of infertility, the effects of mild thyroid dysfunction or thyroid autoimmunity are still unknown. Thyroid function may play a role in female reproduction, which is especially important when the cause of infertility is unknown.

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**Results:** Overall, the median TSH was significantly higher in female patients with infertility than in the control group, 1.4 (0.5) and 1.1 (0.4) mIU/L. The prevalence of positive thyroid peroxidase antibody (TPO-Ab) was higher in infertile women compared to the control group (14% vs. 8%). About 21 (16%) patients had TPO-Ab+ and 99 (84%) patients had TPO-Ab-. On the other hand, the free thyroxine level was not much higher in infertile women than in a control group of women (13 vs. 12). The level of causes of infertility was higher in OD patients (59%) than patients with endometriosis (11%) and tubal (30%).

**Conclusion:** The current study found that thyroid autoimmunity traits are much more common in infertile women than in healthy fertile controls, particularly in the endometriosis subgroup.

**Keywords:** thyroid autoimmunity, thyroid dysfunction, infertility.

## I. INTRODUCTION

Infertility is defined as the lack of conception following a year of regular menstrual cycles and unprotected intercourse. It affects 10–15 percent of marriages in wealthy countries [1]. Female infertility can be caused by endometriosis, tubal disease, or ovulatory dysfunction (OD) [2]. Thyroid hormones obstruct a variety of reproductive functions. Thyroid diseases, such as hypothyroidism and hyperthyroidism, have been

shown to interfere with ovarian function and negatively impact pregnancy outcomes [3]. The question of whether modest thyroid dysfunction or thyroid autoimmunity affects normal female fertility is still unclear.

Thyroid dysfunction is the second most common endocrine condition among women of reproductive age, behind diabetes mellitus, and thyroid autoimmunity (TAI) is the most common autoimmune disorder among these women. The prevalence of hypothyroidism in women of reproductive age is estimated to be 2–4%, with a TAI level of 5–20% [4]. Furthermore, more than 20% of women with thyroid dysfunction have an aberrant menstruation pattern, the most well known of which is oligomenorrhea [3]. The thyroid hormone is a hormone that affects metabolism in almost every tissue in the human body. The availability of thyroid hormone is critical for normal female reproductive. Overt hypothyroidism can result in a blunting of luteinizing hormone (LH) pulsatility, hyperprolactinemia, menstruation, and ovulation abnormalities, and decreased overall fertility, all of which can be reversed by re-establishing a euthyroid state [2]. According to research, even minor thyroid dysfunction or thyroid autoimmunity might harm the female reproductive [3,4]. Several studies have found that infertile women are more likely to have mild hypothyroidism or thyroid autoimmunity [1,3]. Thyroid hormone fluctuation already within the normal range, according to preclinical studies, modulates the stimulatory effects of follicle-stimulating hormone (FSH) on follicular development and apoptosis suppression [5,6]. On the other hand, high thyroid hormone levels may inhibit pre-antral follicle formation by reducing granulosa cell aromatase activity [6,7]. We conducted a retrospective case-control study in a group of infertile women to see if thyroid dysfunction and autoimmune were linked.

## II. OBJECTIVE

The study's objective is to determine the association of thyroid autoimmunity (antithyroglobulin and antithyroid peroxidase) and thyroid dysfunction (hypo- or hyperthyroidism) among women with infertility.

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### III. MATERIALS AND METHODS

*Type of Study:* A retrospective case-control study

*Place of Study:* Gynaecology Department of Patuakhali Medical College Hospital, Bangladesh

*Period of study:* January 2020 to July 2021

*Sample size:* 220 cases

*Data collection method:* Data collected from the patients in a prescribed protocol.

*Data analysis:* Standard statistical tool (SPSS version 23) analyzed all data.

mean age of the women in the control group was  $34 \pm 6$ . We then measured the median thyrotropin (TSH) between our two groups. The median TSH was significantly higher in female patients with infertility than in the control group, 1.4 (0.5) and 1.1 (0.4). The prevalence of positive thyroid peroxidase antibody (TPO-Ab) was higher in infertile women compared to the control group (14% vs. 8%). The free thyroxine level was not much higher in infertile women than in a control group of women (13 vs. 12). See table 1-

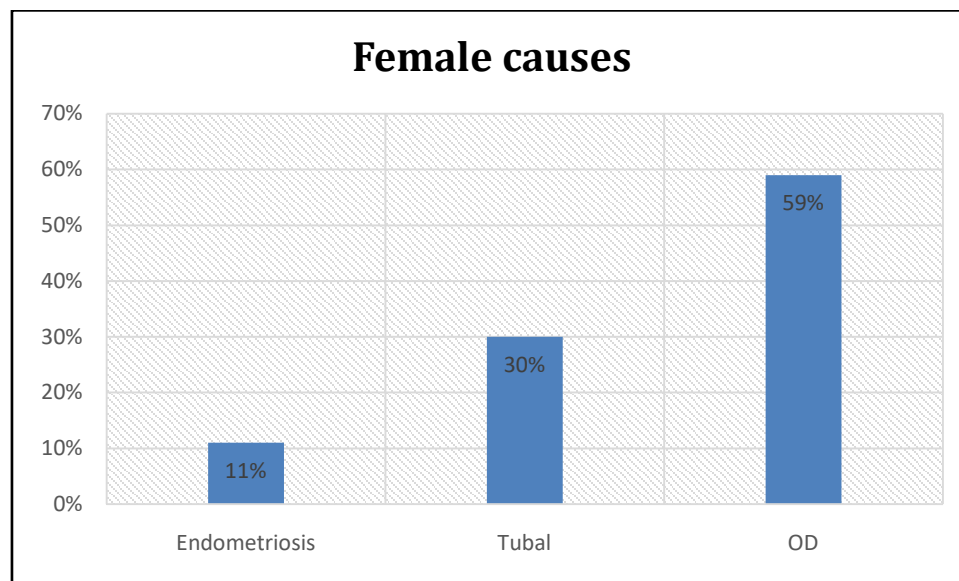
### IV. RESULTS

Table 1 shows that the mean age of the case group consisting the infertile women was  $35 \pm 7$ . The

*Table 1:* Age and thyroid parameters of female infertile patients

Variables	Infertile women N=120	Control group N=100
Age	$35 \pm 7$	$34 \pm 6$
TSH <sup>a</sup>	1.4 (0.5)	1.1 (0.4)
TPO-Ab <sup>b</sup>	17%	9%
FT <sub>4</sub> <sup>a</sup>	13 (3)	12 (4)
95% CI	1.08-4.73	0.72-2.48

In figure 1, the causes of infertility among female patients are observed. The level was higher in OD patients (59%) than patients with endometriosis (11%) and tubal (30%). See figure 1 below-



*Figure 1:* Cause of infertility in female patients with infertility

In figure 2, the pie chart shows the percentage of thyroid dysfunction in women. About 21 (16%) patients had TPO-Ab+ and 99 (84%) patients had TPO-Ab-. See figure 2 here-

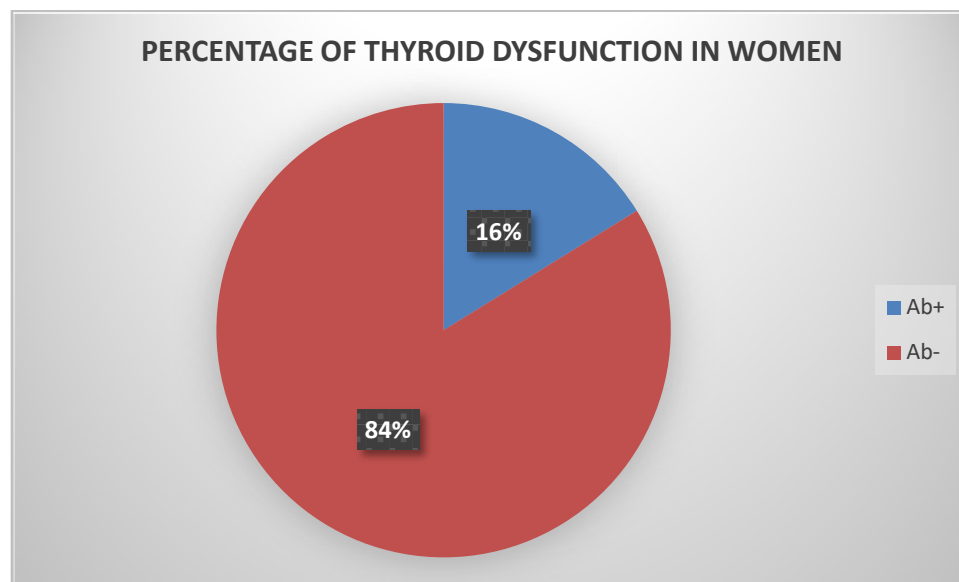


Figure 2: Pie chart of thyroid dysfunction in women

In table 2, it shows the TPO-Ab antibody-positive and antibody-negative patients. The maximum number of patients were TPO-(Ab-)/ antibody negative.

In the control group, 86 patients were TPO-(Ab-)/ antibody negative. See table 2 below-

Table 2: Thyroid dysfunction in antibody-positive and antibody-negative patients as a percentage

Female cause	TPO-Ab (Ab+)	TPO-Ab (Ab-)
Endometriosis	7	19
Tubal	17	42
Ovulatory dysfunction	13	22
Controls	14	86

Table 3 shows the percentages of thyrotropin (TSH) in antibody-positive and antibody-negative in infertile women patients. Here maximum number (17%)

of patients with TSH-ia had Tubal (Ab+), and the maximum number (16%) of patients with TSH-sa had Endometriosis (Ab+). See table 3 below-

Table 3: Thyrotropin (TSH) percentage in antibody-positive and antibody-negative patients

Female cause	TSH-ia	TSH-sa
Endometriosis (Ab+)	3%	16%
Endometriosis (Ab-)	1%	0%
Tubal (Ab+)	17%	15%
Tubal (Ab-)	1%	0%
Ovulatory dysfunction (Ab+)	4%	1%
Ovulatory dysfunction (Ab-)	1%	0%
Controls (Ab+)	1%	0%
Controls (Ab-)	0%	2%

## V. DISCUSSION

In the current study, we looked into whether thyroid autoimmunity and thyroid dysfunction are risk factors for infertility in women. As a result, we systematically screened all female infertility patients. All patients had their anti-TPO, TSH, and FT4 levels tested, and the underlying cause of infertility was determined using strict objective criteria. Positive TPO-Ab antibodies were shown to be more common in patients than in controls, and women with endometriosis had a much higher frequency of positive TPO-Ab antibodies than

controls. Similar findings were reported by Gerhard et al. [8], who found that 44 percent of infertile women with positive thyroid antibodies developed endometriosis, compared to just 9% of women who did not have antibodies. When the findings from Gerhard et al. [8] are considered, they support the concept that autoimmune thyroid disease (AITD) and endometriosis are linked. Such results could back up the theory that an immunological malfunction causes endometriosis.

The tendency toward a higher incidence of TPO-Ab in the two types of female infertility (tubal and OD) remains unclear [9]. TPO-Ab positivity was roughly

6% in women of reproductive age, hypothyroidism was 2%, and hyperthyroidism was 1.3 percent, all of which are close to the present control group prevalence [6,7]. In a recent retrospective study of 299 infertile women in Finland, hypothyroidism (both subclinical and overt) was shown to constitute 4 percent of the overall prevalence of infertility [10].

In our study, subgroup analysis identified 59% of infertile women with OD, 30% among those with tubal infertility, 11% among those with endometriosis. In two separate prospective investigations, increased serum TSH was found in 0.7 percent and 2.3 percent of women with infertility, the majority of whom were infertile due to OD; however, neither study included a control group of healthy fertile women [11,12]. The overall mean serum TSH in women with infertility was considerably higher than in controls in the current study. When compared to antibody-negative women, all antibody-positive women had considerably higher and lowered TSH levels. Thyroid hormones affect granulosa and luteal cells, as well as oocytes, directly. Therefore overt thyroid failure in infertile women has clear clinical implications [10,13]. Thyroid disorders should be treated as soon as feasible. Women with AITD have a substantially increased likelihood of having an early miscarriage, according to research [14]. Early thyroid hormone therapy significantly enhanced the frequency of live births compared to intravenous immunoglobulin delivery throughout pregnancy in women with recurrent abortions and positive TPO-Ab and mild thyroid insufficiency, according to an intervention study [15]. It has previously been shown that women with infertility have a high prevalence of depression and a lower quality of life, including physical and emotional elements [16,17].

## VI. CONCLUSION

The current study found that women with positive TPO-Ab had a considerably higher risk of female infertility, particularly infertility caused by endometriosis. All women with a female cause of infertility should have their TSH, FT4, and thyroid abnormalities tested thoroughly. The effects of thyroid hormone or thyroid autoimmunity on infertility diagnosis were found to differ significantly. This suggests that thyroid hormone or thyroid autoimmunity involvement can be influenced by the various underlying pathophysiological mechanisms involved. Future research is needed to confirm this exploratory study's findings and look into the function of the underlying infertility diagnosis in the relationship between thyroid hormone and female reproduction outcomes.

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# Analysis of Cesarean Section Rate using Robson 10 Group Classification System in a Tertiary Hospital: An Observational Study

By Abhilasha Yadav, Rachna Agrawal, K. Romila Chawang & Ruchika Garg

*Sarojini Naidu Medical College*

**Abstract- Background:** The Cesarean Section rate has increased from 12% in 2000 to 21% in 2015. WHO has recommended a rate between 10% and 15% and introduced The Robson's criteria in the year 2015 as a standardized approach to determine the rate and indications of Cesarean section. To understand this and to implement effective measures to reduce cesarean section rates, WHO issued Robson's implementation manual to monitor and compare cesarean section rates in the same setting over time and among different settings.

**Methods:** This is a cross-sectional study of 5744 women delivering in the Obstetric Department of S.N. Medical College, Agra from April 1st through March 31st, 2020. In this study, demographic data, parity, obstetric history, fetal lie, fetal presentation, gestational age, and number of newborns for each woman were collected, grouped using a flowchart, and categorized into 10 groups. In accordance with recommendations from WHO, data were reported using "Robson's classification Report Table" and quality of data, types of population, and the CS rates were analyzed.

**Keywords:** cesarean section rate, robson's criteria, groups.

**GJMR-E Classification:** NLMC Code: WQ 430



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**Result:** There was an overall CS rate of 26 percent, which is higher than the national average. The size of group 5 (15% in our institution) may be responsible for that. Group 5's contribution is very high (40%), which is another reason for the overall higher CS rate.

**Conclusion:** The reduction of the primary CS rate in groups 1 and 2 will result in a reduction of the overall CS rate.

**Keywords:** cesarean section rate, robson's criteria, groups.

## I. BACKGROUND

Over the last few decades, there has been a progressive increase in the rate of cesarean section deliveries in our country. WHO has recommended that this rate should be between 10% and 15% but the driver behind this trend is not completely understood especially in developing countries.<sup>1,2</sup> Immediate and long-term complications of CS included increased risk of maternal mortality and morbidity, increased need for blood transfusion, longer hospitalization,

postpartum infections, retained placenta, stillbirths, postpartum hemorrhage.

Over the last few decades, there has been a progressive increase in the rate of cesarean section deliveries in our country. WHO has recommended that this rate should be between 10% and 15% but the driver behind this trend is not completely understood especially in developing countries. (1,2). The rising cesarean section trend is a major public health concern due to potential maternal and perinatal risks associated with this. Immediate and long-term complications of CS included increased risk of maternal mortality and morbidity, increased need for blood transfusion, longer hospitalization, postpartum infections, retained placenta, stillbirths, postpartum hemorrhage.

To understand this and to implement effective measures to reduce cesarean section rates, a tool is required to monitor and compare cesarean section rates in the same setting over time and among different settings. Traditionally, at the facility level, we monitor cesarean section rates using the overall percentage of deliveries by cesarean section. But because of some intrinsic differences in hospital factors and infrastructure, a difference in characteristics of the population, and differences in clinical management protocols, this "overall cesarean section rate" becomes difficult to interpret and compare. Ideally, there should be a classification system to monitor and compare cesarean section rates. Such a system should be simple, clinically relevant, accountable, replicable, and verifiable (3,4,5). In 2015, WHO introduced Robson's criteria in the year 2015 as a standardized method to determine the rate and indications of cesarean section and issued an implementation manual(6).

- Obstetric history (parity and previous cesarean section)
- The onset of labor (spontaneous, induced, or cesarean section before the onset of labor)
- Fetal presentation or lie (cephalic, breech, or transverse)
- Number of neonates
- Gestational age (preterm or term).

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## II. MATERIALS AND METHODS

This study is a cross-sectional study of 5744 women delivered in the department of obstetrics of S.N. Medical College, Agra performed from 1<sup>st</sup> April 2020 to 31<sup>st</sup> March 2021. S.N. Medical College is a tertiary referral hospital where around 6000 deliveries take place annually.

All women who underwent cesarean section in the hospital during the specified period were included in the study.

Cases with incomplete information, doubtful gestational age, and laparotomy for uterine rupture were excluded from the study. The identity of women who underwent cesarean section was obtained from the delivery register, admission and discharge register, and operation register. The admission and

discharge register and delivery register contained information about all women who delivered in the hospital regardless of the mode of delivery (vaginal, Caesarean section) while the operation register contained only information about women who underwent Caesarean section. Using the medical registration number of each woman, we accessed all Caesarean section files performed during the study. 10 groups and their characteristics are shown in table 1. Gestational age was categorized as a term ( $\geq 37$  weeks) or preterm ( $< 37$  weeks). Patient's demographic data, patient's parity, obstetric history, the onset of labor, fetal presentation or lie, number of neonates, gestational age were collected. The indications for cesarean section were grouped using a flowchart (figure 1).

*Table 1:* The Robson Classification

1	Nulliparous women with a single cephalic pregnancy, $\geq 37$ weeks gestation in spontaneous labor
2	Nulliparous women with a single cephalic pregnancy, $\geq 37$ weeks gestation who had labor induced or were delivered by cesarean section before labor
2a	Cesarean section performed after induction of labor
2b	Cesarean section performed before onset of labor
3	Multiparous women without a previous cesarean section, with a single cephalic pregnancy, $\geq 37$ weeks gestation in spontaneous labor
4	Multiparous women without a previous cesarean section, with a single cephalic pregnancy, $\geq 37$ weeks gestation who had labor induced or were delivered by cesarean section before labor
4a	Cesarean sections performed after induction of labor
4b	Cesarean sections performed before onset of labor
5	All multiparous women with one or more previous cesarean sections, with a single cephalic pregnancy, $\geq 37$ weeks gestation
5.1	With one previous cesarean section
5.2	With two or more previous cesarean sections
6	All nulliparous women with a single breech pregnancy
7	All multiparous women with a single breech pregnancy including women with previous cesarean section
8	All women with multiple pregnancies including women with previous cesarean section
9	All women with a single pregnancy with a transverse or oblique lie, including women with previous cesarean section
10	All women with a single cephalic pregnancy $< 37$ weeks gestation, including women with previous cesarean section

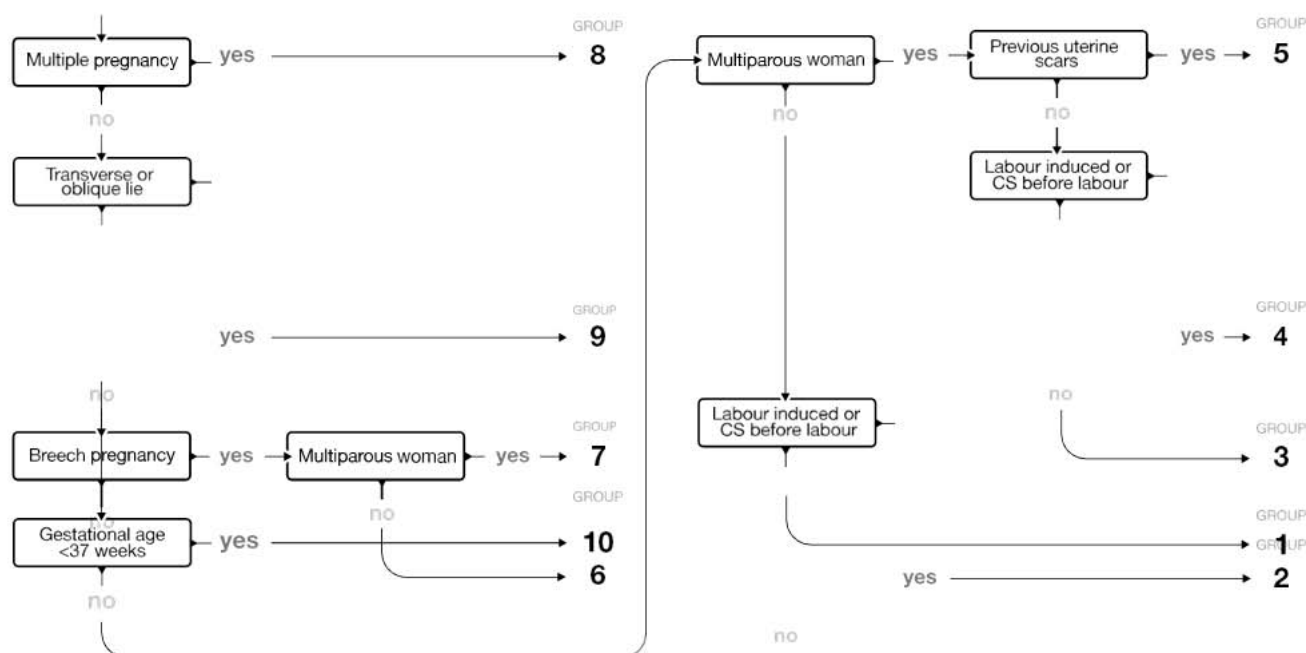
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Figure 1: Flow chart for the classification of women in the Robson Classification

### III. RESULT

To make the most of the information provided by the Robson Classification in local settings and to

allow comparisons between settings, the data is best reported in a standardized way (the "Robson Classification Report Table")<sup>7</sup>

Table 2: The Robson Classification Report Table

Group	Number of CS in group	Number of women in the group	Group Size1 (%)	Group CS rate2 (%)	Absolute group contribution to overall CS rate3 (%)	The relative contribution of a group to overall CS rate4 (%)
1	214	1750	30.43	12.23	3.73	14.21
2	204	603	10.49	33.83	3.55	13.55
3	48	1346	23.43	3.57	0.84	3.19
4	58	259	4.51	22.39	1.01	3.85
5	603	873	15.12	69.07	10.50	40.04
6	60	77	1.34	77.92	1.04	3.98
7	36	82	1.43	43.90	0.63	2.39
8	27	71	1.24	38.02	0.47	1.79
9	39	42	0.73	92.86	0.68	2.59
10	217	741	12.90	29.28	3.78	14.41
<b>Total*</b>	<b>Total number CS 1506</b>	<b>Total number women delivered 5744</b>	<b>100%</b>	<b>Overall CS rate 26.22%</b>	<b>Overall CS rate 26.22%</b>	<b>100%</b>

Unclassifiable: Number of cases and % [Number unclassifiable cases/(Total Number women delivered classified+unclassified)X100]

\* These totals and percentages come from the data in the table.

1. Group size(%)=no of women in the group/total no of women delivered in the hospital x 100

2. Group CS rate(%)=no of CS in the group/total no of women in the group x 100

3. Absolute contribution (%)=no of CS in the group/total no of women delivered in the hospital x 100

4. Relative contribution(%)=no of CS in the group/total no of CS in the hospital x 100



## A. Steps to assess the quality of data

*Table 3:* Steps to assess the quality of data using the Robson Classification Report Table

Steps	Robson guideline	Result	Interpretation
1. The total number of cesarean sections and women delivered in our hospital	These numbers should be the same as the total number of cesarean sections performed and of women delivered in the hospital.	57	We excluded the cases with incomplete data
2. Look at the size of Group 9 i.e. all women with single ton transverse or oblique lie.	It should be less than 1%.	0.73%	It is less than 1%
3. Look at the CS rate of Group 9	It should be 100% by convention.	92.86	3 extremely preterm pregnancies with intrauterine death of fetus were delivered vaginally

## B. Steps to assess the type of population

*Table 4:* Steps to assess the type of population using the Robson Classification Report Table

Steps	Robson guideline	Result	Interpretation
1. Look at the size of Group 1 + 2 i.e. All nulliparous women $\geq 37$ weeks gestation singleton cephalic	This usually represents 35-42% of the obstetric population of most hospitals.	40.9%	It is within the acceptable range
2. Look at the size of Groups 3 + 4 i.e. All multiparous women $\geq 37$ weeks gestation single ton cephalic, without previous CS	This usually represents about 30% of women.	26.2%	The reason for low size of Groups 3 and 4 could be that the size of Group 5 is very high which is accompanied by a high overall CS rate.
3. Look at the size of Group 5. (Multiparous women with previous cesarean section $\geq 37$ weeks gestation with singleton cephalic pregnancy).	It is related to the overall CS rate. Group 5 usually contributes to about half of the total CS rate. In settings with low overall CS rates it is usually under 10%.	15.12%	Overall CS rate is usually related to the size of group 5 and the size of this group is larger ( $> 15\%$ ) if the institute has high CS rate in the past years mainly in Groups 1 and 2.
4. Look at the size of Groups 6 + 7 i.e. Breeches in nulliparous women + breeches in multiparous women	It should be 3-4%	2.77%	It is within the acceptable range
5. Look at the size of Groups 8 Multiples	It should be 1.5 -2%	1.43%	It is nearly within the acceptable range
6. Look at the size of Groups 10 Preterm cephalic and singletons	It should be less than 5% in most normal risk settings.	12.9%	Can be higher in tertiary hospitals as women with high-risk factors are being referred to our hospital. These women require induction of labor, so it is accompanied by a high rate of cesarean section in this group.
7. Look at the Ratio of the size of Group 1 versus Group 2	It is usually 2:1 or higher	2.90	It is acceptable according to Robson.
8. Look at the Ratio of the size of Group 3 versus Group 4	It is always higher than the ratio of Group 1/Group 2 in the same institution. This is a very reliable finding in confirming data quality and culture of the organization.	5.2	The Ratio of group 3:group 4 is larger than the ratio of group 1:group 2 which strongly signifies the reliability of data

9. Look at the Ratio of the size of Group 6 and Group7.	The ratio of nulliparous breech/multiparous breech is usually 2:1 because breeches are more frequent in nulliparous women than in multiparous women.	Ratio 0.94	It can be because of an unusual nullipara/multipara ratio.
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#### C. Steps to assess the rate of cesarean section

*Table 5:* Steps to assess cesarean section rates using the Robson Report Table

Steps	Robson guideline	Result	Interpretation
1. Look at the CS rate for Group1	Rates under 10% are achievable	12.23%	It is slightly higher in our hospital.
2. Look at the CS rate for Group2	Consistently around 20-35%	33.83%	It is within the appropriate range.
3. Look at the CS rate for Group3	Normally, no higher than 3.0%.	3.57%	Slightly higher than 3%
4. Look at the CS rate for Group 4	It rarely should be higher than15%	22.39%	CS rates in Group 4 reflect the size and rates in 4a and 4b. If the size of Group4 is large (there are more cases of prelabour cesarean sections), the overall CS rate in Group 4 is also to be high.
5. Look at the CS rate for Group 5	Rates of 50-60% are considered appropriate.	69.07%	Rates are higher, this is due to a large number of women with 2 or more previous CS.
6. Look at the CS rate for Group8	It is usually around 60%.	38.02%	The lower rate can be due to more number of multiparous twins or due to nulliparous/multiparous with or without a previous scar.
7. Look at the CS rate in Group10	In most populations, it is usually around 30%	29.28%	It is around 30% in our institution
8. Look at the relative contribution of Groups 1,2, and 5 to the overall CS rate	These three groups combined normally contribute to 2/3rd (66%) of all Caesarean sections done in most hospitals.	These three groups combined contributed to 67.8% of all CS	These three groups are contributing to 2/3rd of all CS.
9. Look at the absolute contribution of Group 5 to the overall C.S rate		This group was responsible for 40% of all CS	This indicates that C.S. rates in Groups 1 and 2 have generally been high in previous years, and should be investigated further.

## IV. DISCUSSION

Cesarean sections are becoming more common over the world, with rates rising from 12% in 2000 to 21% in 2015.<sup>8</sup> In India, the caesarean section rate has been steadily growing from 8.5 percent in 2005-2006 to 17.2 percent in 2015-2016, following global trends.<sup>9</sup> Many authors have expressed their satisfaction with this classification and have suggested that it be utilised more widely.<sup>10,11</sup> Madhav Prasad wrote in a 2015 article that now is an ideal moment for India to use the 10-group Robsons classification to rate caesarean sections.<sup>12</sup> The bulk of caesarean sections were found in

groups 2 and 5, according to Deepika Jamwal et al. Group 5 was responsible for 40.3 percent of all caesarean sections, while group 2 was responsible for 29.2%.<sup>13</sup> At a study conducted in a private tertiary care centre in northwest India, Priyanka D. Jogia et al. discovered that group 5 (women with a history of CS) contributed the most (37 percent) to overall surgical deliveries, with group 2 being the second highest contributor (21 percent).<sup>14</sup> Pratima et al conducted a study of 81,784 deliveries (62,336 vaginal and 19,448 Cesarean deliveries) over 3 years. The year-wise CS rate was 22.4%, 23.5% and 25.5%, respectively. The largest contributor was by group 5 followed by group 2 and

group 1. Based on 3-year data, it was predicted in the study that the CS rate will increase by 0.905% annually in the coming 3 years. (15). During the study period, our institution's overall caesarean section rate was 26.22 percent, which looks to be higher than the national norm. Robson group 5 was the most significant single contribution to our institution's CS rate. Caesarean section rate in group 1 was higher than recommended i.e. 12.23% (rate <10% are achievable) and in group 3 CS rate was 3.57% against the recommended rate of <3%. In group 5 the caesarean section rate between 50-60% is recommended but in our institution CS rate in group 5 was 69% as a large number of women with previous 2 or more caesarean sections were being admitted. The absolute contribution of group 5 is very high (40%), this indicates high CS rates. The size of group 5 is frequently connected to the overall caesarean section rate. The size of group 5 in our study was 15%, which explains our institution's overall increased caesarean section rate. It's also worth noting that Robson group 10 has grown in size (preterm deliveries). Because women with high-risk conditions are referred to our hospital, Robson group 5 can be greater in tertiary hospitals. Induction of labour is necessary for these women, hence there is a high rate of caesarean section in this group. In group 1 and group 2 in previous years.

## V. CONCLUSION

Reducing the primary caesarean section rate in group 1 and group 2 will reduce the overall caesarean section rate in the institution.

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# Uterine Leiomyosarcoma in a Young Unmarried Lady- A Case Report

By Begum Monowara, Begum Tahmina, Zihan Nazia & Hossain Shahlee

**Abstract-** Leiomyosarcoma of the uterus is a very rare malignancy. It arises from the smooth muscles of the uterus. Very few cases on uterine leiomyosarcoma have been published so far. We report a case of a 23-year-old unmarried female who was having severe menorrhagia and was diagnosed later as a case of uterine leiomyosarcoma. The final diagnosis of leiomyosarcoma was made by histopathology. The only curative treatment of leiomyosarcoma of the uterus is surgery. The prognosis completely depends on the extension and histological characteristics like mitotic index, during the time of diagnosis.

**Keywords:** leiomyosarcoma of the uterus; menorrhagia; uterine malignancy.

**GJMR-E Classification:** NLMC Code: WP 440



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# Uterine Leiomyosarcoma in a Young Unmarried Lady- A Case Report

Begum Monowara <sup>α</sup>, Begum Tahmina <sup>α</sup>, Zihan Nazia <sup>ρ</sup> & Hossain Shahlee <sup>ω</sup>

**Abstract-** Leiomyosarcoma of the uterus is a very rare malignancy. It arises from the smooth muscles of the uterus. Very few cases on uterine leiomyosarcoma have been published so far. We report a case of a 23-year-old unmarried female who was having severe menorrhagia and was diagnosed later as a case of uterine leiomyosarcoma. The final diagnosis of leiomyosarcoma was made by histopathology. The only curative treatment of leiomyosarcoma of the uterus is surgery. The prognosis completely depends on the extension and histological characteristics like mitotic index, during the time of diagnosis.

**Keywords:** leiomyosarcoma of the uterus; menorrhagia; uterine malignancy.

## I. INTRODUCTION

Leiomyosarcoma of the uterus is a very rare malignancy. Its prevalence is only 1%-2% of the uterine malignancy especially after the menopause. It arises from the smooth muscle of the uterus. They are highly aggressive in nature and carry very poor prognosis. At the same time, it is very difficult to define the treatment modalities due to its diverse pathological presentations which often creates diagnostic dilemma. We report a case of a 23-year-old unmarried female who was having severe menorrhagia and was diagnosed later as a case of uterine leiomyosarcoma after the surgical intervention.

## II. CASE PRESENTATION

A 23-year-old unmarried Bangladeshi lady was admitted through the OPD of Evercare Hospital Dhaka on 6 September, 2020 as a diagnosed case of fibroid uterus. She had severe menorrhagia which started since November, 2019. During this period, she was transfused several units of blood. She had not suffered either from any long-term illness or from any chronic disease. She had no family history of such malignancies.

### a) On examination

Patient was ill looking but cooperative. Her body built was normal. She was hemodynamically stable. She was mildly anemic. Per abdominal examination, uterus was palpable about 14 week's size of pregnant uterus. The mass was mobile which non tender was. The

overlying skin was normal. Per vaginal examination was not done as she was unmarried.

### b) Investigations

Full blood count showed that hemoglobin was 11.0 gm/dl, WBC was  $9.35 \times 10^9/L$  and Platelet was  $705 \times 10^9/L$ . On ultrasonography dated 26 August 2020, uterus was bulky measuring about  $15.0 \text{ cm} \times 5.5 \text{ cm}$ . Fairly large mixed echogenic predominantly hypoechoic focal lesion involving the whole cervix and lower part of the body of the uterus measuring about  $8.5 \text{ cm} \times 5.3 \text{ cm}$  (Figure 1). Endometrium was thickened about 20.1 mm. Both the ovaries were normal.

She was planned for laparoscopic surgery. On 7 September 2020, she underwent laparo-hysteroscopic myomatous polypectomy and specimen was sent for histopathology which revealed leiomyosarcoma (Grade-I). Staging CT chest and abdomen were unremarkable.

### c) Operative findings

She underwent laparoscopic procedure and hysteroscopic resection of myomatous polyp. During laparoscopic procedure, uterus was found enlarged about 14 weeks size and bulged over the posterior uterine wall, both the fallopian tubes and ovaries were looking healthy. Intracapsular vasopressin was injected through posterior uterine wall. A small incision was given over the lower part of posterior uterine wall to get reach of myoma. But finally planned laparoscopic procedure was abandoned. Later we approached per vaginally. Her vaginal examination revealed a large degenerative myomatous polyp about  $8 \text{ cm} \times 6 \text{ cm}$  protruding through cervix and occupying the whole vagina. It was friable. This large polyp was arising from lower part of uterus and cervix and was attached to uterine wall with broad pedicle. The myoma was excised per vaginally though complete removal was not possible. Then hysteroscope was introduced for resection of rest of the polyp and was sent for histopathology. Histopathology report showed leiomyosarcoma. On 14 September 2020, she underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy with pelvic lymph node sampling. Uterus was bulky in size. Frozen section biopsy was sent. It was found negative for malignancy. Uterus with both adnexa and pelvic lymph nodes were sent for histopathological examination.

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d) *On histopathological examination*

Anaplastic spindle epithelioid cells showed marked pleomorphism with many mitotic figures (Figure 2a, b). It was diagnosed to be a case of leiomyo-

sarcoma (high grade). Lympho-vascular invasion was not identified.



Figure 1: Ultrasonogram of the uterus showing fibroid.

e) *Postoperative period*

The postoperative period was uneventful. The patient was discharged after five days.

### III. DISCUSSION

Leiomyosarcoma of the uterus is an uncommon malignancy. Its account for only 1%-2% of the uterine cancer. The annual incidence is only 0.64 per 100,000 women. Leiomyosarcoma can occur anywhere in the pelvic cavity including the cervix and urinary bladder. But it is more commonly developed in the uterus which was also seen in our case [1]. Mostly occur in post-menopausal women over the age of 60 who usually develop abnormal vaginal bleeding (56%), palpable lower abdominal mass (54%) as well as pain (22%). It sometimes may resemble with the leiomyoma and often very difficult to distinguish between the two tumors before the surgery [2]. The patient presented with the complaints of severe menorrhagia. Uterine fibroids do not usually turn into malignant leiomyomas. Leiomyosarcomas may coexist within the fibroid uterus. About 0.5% of the hysterectomy cases for uterine fibroids are having leiomyosarcomas [3]. It is very difficult to diagnose leiomyosarcoma accurately without surgery. Because leiomyosarcoma of the uterus is associated with multiple fibroids and most of the time it is difficult to identify which ones should be biopsied [4]. Magnetic Resonance Imaging (MRI) might help in the diagnosis but less accurate. Leiomyosarcoma of the uterus are very aggressive in nature with high rates of recurrence. It develops from the myometrium or a vessels. The diagnosis of uterine sarcoma is confirmed by histological examination of entire uterus as seen in our case. The recommended treatment is total hysterectomy. But bilateral salpingo-oophorectomy and lymph nodes are not recommended since lymph nodes

involvement is very rare [5]. It is commonly spread by hematogenous route. Lymphatic spread is very rare. Up to 70% of recurrences occur in stage I and II disease. The most of the recurrences occur distally that is in the upper abdomen or lungs [6-8]. The rate of survival closely depends on the stage of disease at times of diagnosis. Fifty percent of the patients with stage I disease usually survive five years on the other hand only 8%-12% with stage II-IV disease survive five years [7]. Overall, the five-year survival rate is about 30%-50%. Patients with local recurrences can be managed with surgery. Isolated pulmonary metastasis can also be treated by resection [9].

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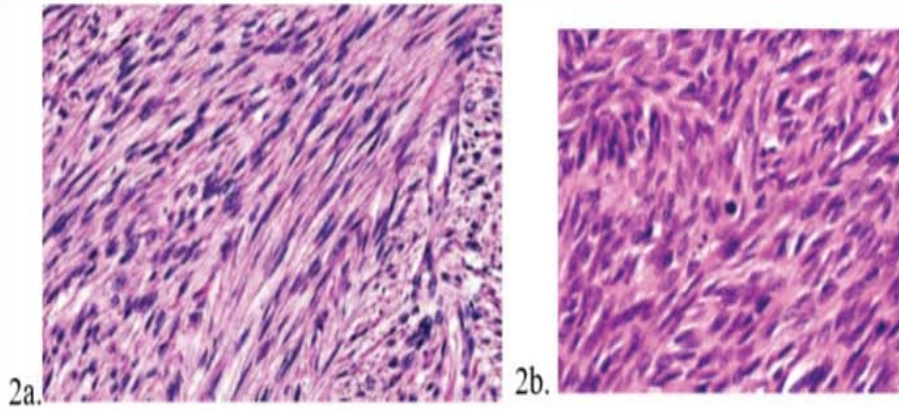


Figure 2: a) and b) Histological pictures of leiomyosarcoma.

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Plagiarized content will not be considered for publication. We reserve the right to inform authors' institutions about plagiarism detected either before or after publication. If plagiarism is identified, we will follow COPE guidelines:

Authors are solely responsible for all the plagiarism that is found. The author must not fabricate, falsify or plagiarize existing research data. The following, if copied, will be considered plagiarism:

- Words (language)
- Ideas
- Findings
- Writings
- Diagrams
- Graphs
- Illustrations
- Lectures





- Printed material
- Graphic representations
- Computer programs
- Electronic material
- Any other original work

## AUTHORSHIP POLICIES

Global Journals follows the definition of authorship set up by the Open Association of Research Society, USA. According to its guidelines, authorship criteria must be based on:

1. Substantial contributions to the conception and acquisition of data, analysis, and interpretation of findings.
2. Drafting the paper and revising it critically regarding important academic content.
3. Final approval of the version of the paper to be published.

### Changes in Authorship

The corresponding author should mention the name and complete details of all co-authors during submission and in manuscript. We support addition, rearrangement, manipulation, and deletions in authors list till the early view publication of the journal. We expect that corresponding author will notify all co-authors of submission. We follow COPE guidelines for changes in authorship.

### Copyright

During submission of the manuscript, the author is confirming an exclusive license agreement with Global Journals which gives Global Journals the authority to reproduce, reuse, and republish authors' research. We also believe in flexible copyright terms where copyright may remain with authors/employers/institutions as well. Contact your editor after acceptance to choose your copyright policy. You may follow this form for copyright transfers.

### Appealing Decisions

Unless specified in the notification, the Editorial Board's decision on publication of the paper is final and cannot be appealed before making the major change in the manuscript.

### Acknowledgments

Contributors to the research other than authors credited should be mentioned in Acknowledgments. The source of funding for the research can be included. Suppliers of resources may be mentioned along with their addresses.

### Declaration of funding sources

Global Journals is in partnership with various universities, laboratories, and other institutions worldwide in the research domain. Authors are requested to disclose their source of funding during every stage of their research, such as making analysis, performing laboratory operations, computing data, and using institutional resources, from writing an article to its submission. This will also help authors to get reimbursements by requesting an open access publication letter from Global Journals and submitting to the respective funding source.

## PREPARING YOUR MANUSCRIPT

Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.



### ***Manuscript Style Instruction (Optional)***

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

### ***Structure and Format of Manuscript***

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

- a) A title which should be relevant to the theme of the paper.
- b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
- c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
- d) An introduction, giving fundamental background objectives.
- e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
- f) Results which should be presented concisely by well-designed tables and figures.
- g) Suitable statistical data should also be given.
- h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

- i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
- j) There should be brief acknowledgments.
- k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and suggestions to improve brevity.



## FORMAT STRUCTURE

***It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.***

All manuscripts submitted to Global Journals should include:

### **Title**

The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

### **Author details**

The full postal address of any related author(s) must be specified.

### **Abstract**

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

### **Keywords**

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, "What words would a source have to include to be truly valuable in a research paper?" Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

### **Numerical Methods**

Numerical methods used should be transparent and, where appropriate, supported by references.

### **Abbreviations**

Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

### **Formulas and equations**

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

### **Tables, Figures, and Figure Legends**

Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.



## Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

### PREPARATION OF ELETRONIC FIGURES FOR PUBLICATION

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution at final image size ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs): >350 dpi; figures containing both halftone and line images: >650 dpi.

Color charges: Authors are advised to pay the full cost for the reproduction of their color artwork. Hence, please note that if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a Color Work Agreement form before your paper can be published. Also, you can email your editor to remove the color fee after acceptance of the paper.

### TIPS FOR WRITING A GOOD QUALITY MEDICAL RESEARCH PAPER

**1. Choosing the topic:** In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

**2. Think like evaluators:** If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

**3. Ask your guides:** If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

**4. Use of computer is recommended:** As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

**5. Use the internet for help:** An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.



**6. Bookmarks are useful:** When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

**7. Revise what you wrote:** When you write anything, always read it, summarize it, and then finalize it.

**8. Make every effort:** Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

**9. Produce good diagrams of your own:** Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

**10. Use proper verb tense:** Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

**11. Pick a good study spot:** Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

**12. Know what you know:** Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

**13. Use good grammar:** Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

**14. Arrangement of information:** Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

**15. Never start at the last minute:** Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

**16. Multitasking in research is not good:** Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

**17. Never copy others' work:** Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

**18. Go to seminars:** Attend seminars if the topic is relevant to your research area. Utilize all your resources.

**19. Refresh your mind after intervals:** Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.



**20. Think technically:** Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

**21. Adding unnecessary information:** Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

**22. Report concluded results:** Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

**23. Upon conclusion:** Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium through which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

## INFORMAL GUIDELINES OF RESEARCH PAPER WRITING

### Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

### Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

*The introduction:* This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

### The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

### General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

**To make a paper clear:** Adhere to recommended page limits.





### *Mistakes to avoid:*

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

### **Title page:**

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

**Abstract:** This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

*Reason for writing the article—theory, overall issue, purpose.*

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

### **Approach:**

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

### **Introduction:**

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.



*The following approach can create a valuable beginning:*

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

#### **Approach:**

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

#### **Procedures (methods and materials):**

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

#### **Materials:**

*Materials may be reported in part of a section or else they may be recognized along with your measures.*

#### **Methods:**

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

#### **Approach:**

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

#### **What to keep away from:**

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.



**Results:**

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

**Content:**

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

**What to stay away from:**

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

**Approach:**

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

**Figures and tables:**

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

**Discussion:**

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."



Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

#### **Approach:**

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

### THE ADMINISTRATION RULES

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

*Please read the following rules and regulations carefully before submitting your research paper to Global Journals Inc. to avoid rejection.*

*Segment draft and final research paper:* You have to strictly follow the template of a research paper, failing which your paper may get rejected. You are expected to write each part of the paper wholly on your own. The peer reviewers need to identify your own perspective of the concepts in your own terms. Please do not extract straight from any other source, and do not rephrase someone else's analysis. Do not allow anyone else to proofread your manuscript.

*Written material:* You may discuss this with your guides and key sources. Do not copy anyone else's paper, even if this is only imitation, otherwise it will be rejected on the grounds of plagiarism, which is illegal. Various methods to avoid plagiarism are strictly applied by us to every paper, and, if found guilty, you may be blacklisted, which could affect your career adversely. To guard yourself and others from possible illegal use, please do not permit anyone to use or even read your paper and file.

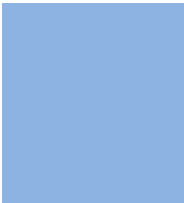


CRITERION FOR GRADING A RESEARCH PAPER (COMPILATION)  
BY GLOBAL JOURNALS

Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals.

Topics	Grades		
	A-B	C-D	E-F
<i>Abstract</i>	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
<i>Introduction</i>	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
<i>Methods and Procedures</i>	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
<i>Result</i>	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
<i>Discussion</i>	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
<i>References</i>	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring





# INDEX

---

---

## A

Abandoned · 19

---

## C

Cephalic · 13, 14, 16

Conception · 1, 3, 4, 5, 7

---

## F

Follicle · 7

---

## M

Malignancy · 19, 20

Meiotic · 3

---

## P

Placental · 3

---

## R

Resemble · 20

---

## T

Translocation · 3, 4





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