Dr. Alpesh Gandhi
President

Dr. Atul Ganatra
Vice President

Dr. Jaydeep Tank
Secretary

Dr. Nandita Palshetkar
Imm. Past President

Dr. Rajat Mohanty
Past V President

Dr. Meena Samant
Chairperson
Clinical Research Committee
## Composition of the committee

**Advisors**
- Dr Alpesh Gandhi
- Dr Nandita Palshetkar
- Dr P C Mahapatra
- Dr Sanjay Gupte
- Dr Suchitra Pandit
- Dr Leela Vyas
- Dr Nozer Sheriar
- Dr Hiralal Konar
- Dr Anita Singh
- Dr Abha Rani
- Dr Vinita Das
- Dr Yashodhara Pradeep
- Dr Alka Pandey
- Dr Ashok Kumar
- Dr Durga Shankar Dash

**National Coordinator**
- Dr A. G. Radhika

**East Zone Coordinator**
- Dr Archana Kumari

**West Zone Coordinator**
- Dr Anupama Dave

**North Zone Coordinator**
- Dr Kanchan Prasad

**South Zone Coordinator**
- Dr. Rekha Rajendrakumar

### EAST ZONE:
- Dr. Hemani Heidi Sinha (PATNA), Dr. Vinita Singh (JAMSHEDPUR), Dr. Amita Sinha (PATNA), Dr. Prashant Kumar Deka (Assam), Dr. Mukta Agarwal (PATNA), Dr. Suruchi Smriti (MOTIHARI), Dr. Divya Suman (PATNA), Dr Priyankur Roy (Siligudi), Dr Saumya Nanda (ODISHA), Dr Hafiz ur Rahman (Gangtok), Dr Kalpana Singh (Patna), Dr Apoorba Dutta, Dr Prabhati Keshari (Bhagalpur)

### WEST ZONE:
- Dr Sonal Richharya (JABALPUR), Dr Swati Bhargav (INDORE), Dr. Sonal Shukla (INDORE), Dr. Hema Dhumale (Bhilai), Dr P Kabra (YAWATMA)

### NORTH ZONE:
- Dr Renu Tondon (KANPUR), Dr Vani Puri (GAZIABAD), Dr Uma Pandey (VARANASI), Dr Taruna Bhargav (NOIDA), Dr Seema Thakur (New Delhi), Dr Alpana Kansal (Ghaziabad), Dr Smriti Agarwal (Lucknow), Dr Rashmi Vyas

### SOUTH ZONE:
- Dr. Shruthi (TELANGANA), Dr Uma (VIJAYWADA), Dr Nivedita Jha (Puducheri), Dr Phani Kumari (Rajahmundry), Dr Jyoti Mahesh (Tumkur), Dr Ramaraju
Dear friends,

Greetings from team FOGSI CRC !!
We have come out with yet another issue of newsletter carrying excellent updated reads and Glimpses of our activities.

This year CRC work along with the theme #saynotovawg and tried to create awareness on digital and virtual platforms. Along with posters, messages and talks we also released a booklet on women safety, this booklet briefly informs about legal help on different aspects of violence against women and consist the information regarding help groups and NGOs working in this field.

The second wave of COVID has brought new difficulties and challenges, so, wishing more strength and endurance to us.

Happy Reading !!!

Dr. Kalpana Singh
Dr. Archana Kumari
Dr. Divya Suman
Dr. Kalpana Singh
Why research is important?

I believe in innovation and that the way you get innovation is you fund research and you learn the basic facts."

- Bill Gates

If I were to define utility of research, it would be—research is something that can be applied to real world situations, enhance knowledge of mankind in a way that can address world problems. It would sound familiar if one were to recall the iconic dialogue from a hugely successful Hindi movie 3 idiots where students were asked to answer the question: what a machine is. In way of fundamental element of knowledge- the answer was: it is something that reduces human effort. Now look at the classical purpose of research: it is to inform action, gather evidence for theories, and develop knowledge in a field of study. This sounds quite academic but from a utilitarian perspective, research is merely something that makes the fruits of the human efforts most productive and can improve human lives and enable survival for at least some humans. It is always possible that some research might not be universally welfare improving, like research on atomic bombs but some would still be beneficial in terms of power and deterrence for conflict to others. Importantly, how to minimize the fallout of something like proliferation of arms would itself get answers from research.

Research is required not just for students and academics but for all professionals and nonprofessionals alike and medicine is the area where it probably applies the most. Well-conducted research is vital to the success of health programs, starting from program development to providing the foundation for effective policies and then to implementation.

Research addresses the fundamental situation of scarcity. Take any policy, for example government of India mandate on fortification for improving overcoming micronutrient deficiency. As much one would like, resources would always be limited and choices need to be made among different options. Should the government choose biofortification or supplementation instead? There are costs and benefits associated with each. How would choices be made in a world with competing options, an issue that arises in all decisions relating to health services as well. Here, only research can be the friend, philosopher, guide and most importantly the problem solver in this situation. If there is no research, there are no informed solutions and no evidence-based decisions. Research is what allows we the doctors to decide how to best treat patients, what leads to inventions and
innovations related to new medicines, new procedures and new tools and equipment. Without research, we would not be able to decide if new treatments are better than our current treatments. Even if it were a basic question like role of sleep-in learning outcomes only research has been able to give us knowledge and assess its quantitative and qualitative role.

One of the afflictions related to suboptimal choices being made in India and the policy ineffectiveness, one can quickly point finger to a lack of research behind decisions. Even when one sees the decisions of courts in India, when compared with developed countries (because of all the research done over centuries) like the United States, the research quotient of the judgments is comparatively low. Research involves the process of returning again and again to the question from different perspective that lays the foundation for success by being flexible and open to change leading to better choices or at least recommendations for it.

As explained by lifestyle coach Brunson, the reason for success of Oprah Winfrey show one of the most successful programs in the world is because Oprah spends a disproportionate amount of her time gathering information from communities of people outside of her core (different age groups, social classes, ethnicities, education levels, careers, etc.) and then she shares that information within her community." This kind of effort is what makes research. Research is needed to understand issues, understand people, create and understand fiction or stories. Good everything be it success in business, success in health or success in life is based on research. It is indispensable for helping oneself, helping others, raising personal awareness as well as social consciousness in the times that we live in with biases, propaganda, and fake news. It is pertinent to close by the following quote. But there is no convincing evidence that memory practice and other cognitively stimulating activities are sufficient to prevent Alzheimer disease; it is not just a case of “use it or lose it.” Go ahead and do research.

Dr. Manju Gita Mishra

- Ex-Professor of Obstetrics and Gynaecology, PMCH, Patna.
- President ISOPARPB 2014-2016.
- Chairperson Medical Education Committee, FOGSI -2007-09.
- Recipient of:
  Kanak Goyal Award
  C.L. Jhaveri Family Planning Award
  B.C. ROY Award
  R. K. Menda Community Service Award
Sample Size In Clinical Research: Size Matters

Dr Meena Samant
Senior consultant and HOD Dept of obs & gynae
Kurji Holy Family Hospital Patna

Medical research is done to find a solution to a particular problem i.e., the research question and the answer of this question is based on statistics. In an ideal situation, the entire population should be studied but this is almost impossible. Other than census, which is conducted on each and every person of the population, all other studies are performed on limited subjects drawn from the concerned population known as “sample population”. This is the sub-population, to be studied in order to draw an inference from a reference population (a population to which the findings of the Study are to be generalized).

Sample size calculations is necessary for approval of research projects, clearance from ethical committees, approval of grant from funding bodies, publication requirement for journals and most important of all justify the authenticity of study results. Whatever be the aim, one can draw a precise and accurate conclusion only with an appropriate sample size. A smaller sample will give a result which may not be sufficiently powered to detect a difference between the groups and the study may turn out to be falsely negative leading to a type II error. A study on a small sample is quite tempting for obvious reasons, but it is a waste of time and money as the result will be invariably inconclusive. A very large sample size is also not recommended as it has its own consequences. Firstly, the Study will be difficult and costly, time consuming and less of accuracy. Secondly, recruiting more subjects than required can also be termed as unethical as the patients participate in a study with faith and an altruistic motive which should not be misutilized. Thirdly, in randomized controlled trials more people will be denied a better regimen and will get a placebo or an inferior treatment due to design of the study. These valid reasons are enough to justify proper sample size estimation before the start of any study.

One of frequently asked question by medical students/researchers is how to determine the sample size. Determining the sample size for a study is a crucial component. The goal is to include sufficient numbers of subjects so that statistically significant results can be detected. Sample size determination is the mathematical estimation of the number of subjects/units to be included in a study. When a representative sample is taken from a population, the finding are generalized to the population. Optimum sample size determination is required to allow appropriate analysis, to provide desired level of accuracy and to allow validity to the significance test. Approaches for estimating sample size depend primarily on the study design and
the main outcome measure of the study. There are distinct approaches for calculating sample size for different study designs & different outcome measures. Sample size can be addressed at two stages, firstly, while designing the Study and information on some parameters and at the stage of interpretation of the result.

Though sample size calculation may vary based upon the type of study design, the basic concept remains the same. The three main factors which must be considered are \(\alpha\)-error, \(\beta\)-error and clinically significant difference or the effect size. Type I error or \(\alpha\)-error is failure to accept the null hypothesis when it is actually true. Usually it is set at 5%. The sample size has to be increased if this value has to be lowered. Type II error or \(\beta\)-error is failure to reject the null hypothesis when it is not true. By convention, it can be set at 20%, 10% or 5%. Power of the study is equal to 1-type II error; hence any study should be at least 80% powered. The sample size increases when the power of study is increased from 80% to 90% or 95%. The third factor is the effect size. A small clinically significant difference is difficult to identify and needs a larger sample size as compared to a study with a larger clinically significant difference. The other factors which need to be considered are standard deviation for quantitative measurements, margin of error and attrition rate. These values are either known from literature or can be decided by a pilot study or by reasonable guess work. Before, landing on formula for sample size, understanding of few facts and terms is important. As, the types of measurements in a research are Random error, Systematic error (bias), Precision (reliability), Accuracy (Validity).

**Random error:** Errors that occur by chance. Sources are sample variability, subject to subject differences & measurement errors. These can be reduced by averaging, increasing sample size, repeating the experiment.

**Systematic error:** Deviations not due to chance alone. Several factors, e.g. patient selection criteria may contribute. It can be reduced by good study design and conduct of the experiment.

**Precision:** The degree to which a variable has the same value when measured several times. It is a function of random error.

**Accuracy:** The degree to which a variable actually represent the true value. It is function of systematic error.

**Power:** This is the probability that the test will correctly identify a significant difference, effect or association in the sample should one exist in the population. Sample size is directly proportional to the power of the study. The larger the sample size, the study will have greater power to detect significance difference, effect or association.

**Effect size:** Is a measure of the strength of the relationship between two variables in a population. The bigger the size of the effect in the population, the easier it will be to find out.

**Design effect:** Geographic clustering is generally used to make the study easier & cheaper to perform. The effect on the sample size depends on the number of clusters & the variance between & within the cluster.
In practice, this is determined from previous studies and is expressed as a constant called ‘design effect’ often between 1.0 & 2.0. The sample sizes for simple random samples are multiplied by the design effect to obtain the sample size for the cluster sample.

Generating sample size formula requires (i) specify the amount of confidence we wish to have, (ii) estimate the variance in the population, and (iii) specify the level of desired accuracy we want.

PROCEDURE FOR CALCULATING SAMPLE SIZE

There are 3 procedures that could be used for calculating sample size:

Use of formulae

Ready-made tables

Computer software

Requirements for sample size calculations

\( \mu/p = \text{mean/proportion of interest. } \mu_0/p_0 = \text{null hypothesis mean/proportion. } d = \text{range of confidence interval (CI).} \)

\( u = \text{one –sided percentage point of normal distribution corresponding to 100%-power.} \)

\( v = \text{two-sided percentage point of normal distribution corresponding to required significance level.} \)

TYPICAL VALUES FOR SIGNIFICANCE LEVEL AND POWER

<table>
<thead>
<tr>
<th>Significance level</th>
<th>5%</th>
<th>1%</th>
<th>0.1%</th>
<th>80%</th>
<th>85%</th>
<th>90%</th>
<th>95%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.96</td>
<td>2.58</td>
<td>3.29</td>
<td>0.84</td>
<td>1.04</td>
<td>1.29</td>
<td>1.64</td>
</tr>
</tbody>
</table>

Sample size for The Mean:

\[ n = \frac{Z^2 \times (\text{var})^2}{(e)^2} \]

Where

\( Z = \text{confidence level at 95% (standard value of 1.96) } \)

\( \text{var} = \text{Variance of population} \)

\( e = \text{Allowable error} \)

Sample Size for Proportions & Prevalence:

\[ n = \frac{Z^2 \times p(1-p)}{(e)^2} \]

Where

\( Z = \text{confidence level at 95% (standard value of 1.96) } \)

\( p = \text{Estimated prevalence or proportions of project area} \)

\( e = \text{range of CI} \)

Sample size for two means

\[ (u+v)^2(\sigma^2 1 + \sigma^2 2)/(\mu1 - \mu2)^2 \]

\( \mu1-\mu2 = \text{Difference between means; } \sigma 1 + \sigma 2 = \text{Standard deviation} \)

\( u = \text{one –sided percentage point of normal distribution corresponding to 100%-power.} \)

\( v = \text{two-sided percentage point of normal distribution corresponding to required significance level.} \)
Use of computer softwares for sample size calculation

The following softwares can be used for calculating sample size:

Epi-info (epiinfo.codeplex.com)
nQuery (nquery.codeplex.com)
STATA (www.stata.com)
SPSS (www.spss.co.in)

Using readymade tables:

How large a sample of patients should be followed up if an investigator wishes to estimate the incidence rate of a disease to within 10% of its true value with 95% confidence?

The table shows that for $e=0.10$ & confidence level of 95%, a sample size of 385 would be needed.

This table can be used to calculate the sample size making the desired changes in the relative precision & confidence level e.g. if the level of confidence is reduced to 90%, then the sample size would be 271.

Such tables that give ready made sample sizes are available for different designs & situations.

### Table 3: Estimating an incidence rate with specified relative precision (Formula: $n = \left(\frac{Z}{e}\right)^2$)

<table>
<thead>
<tr>
<th>Relative precision ($\rho$)</th>
<th>99%</th>
<th>95%</th>
<th>90%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>66358</td>
<td>35417</td>
<td>27061</td>
</tr>
<tr>
<td>0.02</td>
<td>16590</td>
<td>9605</td>
<td>6766</td>
</tr>
<tr>
<td>0.03</td>
<td>7374</td>
<td>4269</td>
<td>3007</td>
</tr>
<tr>
<td>0.04</td>
<td>4148</td>
<td>2402</td>
<td>1602</td>
</tr>
<tr>
<td>0.05</td>
<td>2655</td>
<td>1537</td>
<td>1063</td>
</tr>
<tr>
<td>0.06</td>
<td>1644</td>
<td>1068</td>
<td>752</td>
</tr>
<tr>
<td>0.07</td>
<td>1356</td>
<td>878</td>
<td>593</td>
</tr>
<tr>
<td>0.08</td>
<td>1057</td>
<td>601</td>
<td>423</td>
</tr>
<tr>
<td>0.09</td>
<td>820</td>
<td>475</td>
<td>335</td>
</tr>
<tr>
<td>0.10</td>
<td>664</td>
<td>385</td>
<td>271</td>
</tr>
<tr>
<td>0.12</td>
<td>461</td>
<td>267</td>
<td>188</td>
</tr>
<tr>
<td>0.14</td>
<td>339</td>
<td>197</td>
<td>139</td>
</tr>
<tr>
<td>0.16</td>
<td>260</td>
<td>151</td>
<td>106</td>
</tr>
<tr>
<td>0.18</td>
<td>205</td>
<td>110</td>
<td>84</td>
</tr>
<tr>
<td>0.20</td>
<td>166</td>
<td>97</td>
<td>68</td>
</tr>
<tr>
<td>0.22</td>
<td>136</td>
<td>80</td>
<td>56</td>
</tr>
<tr>
<td>0.24</td>
<td>116</td>
<td>67</td>
<td>47</td>
</tr>
<tr>
<td>0.26</td>
<td>99</td>
<td>57</td>
<td>41</td>
</tr>
<tr>
<td>0.28</td>
<td>85</td>
<td>50</td>
<td>35</td>
</tr>
<tr>
<td>0.30</td>
<td>74</td>
<td>45</td>
<td>31</td>
</tr>
<tr>
<td>0.32</td>
<td>65</td>
<td>40</td>
<td>27</td>
</tr>
<tr>
<td>0.34</td>
<td>58</td>
<td>34</td>
<td>24</td>
</tr>
<tr>
<td>0.36</td>
<td>52</td>
<td>30</td>
<td>21</td>
</tr>
<tr>
<td>0.38</td>
<td>46</td>
<td>27</td>
<td>19</td>
</tr>
<tr>
<td>0.40</td>
<td>42</td>
<td>25</td>
<td>17</td>
</tr>
<tr>
<td>0.42</td>
<td>38</td>
<td>22</td>
<td>16</td>
</tr>
<tr>
<td>0.44</td>
<td>35</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>0.46</td>
<td>32</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>0.48</td>
<td>29</td>
<td>17</td>
<td>12</td>
</tr>
</tbody>
</table>

Sample size calculation in cross sectional study

In cross-sectional studies the aim is to estimate the prevalence of unknown parameter(s) from the target population using a random sample. So an adequate sample size is needed to estimate the population prevalence with a good precision.

To calculate this adequate sample size there is a simple formula, however it needs some practical issues in selecting values for the assumptions required in the formula too and in some situations, the decision to select the appropriate values for these assumptions are not simple. The following simple formula would be used for calculating the adequate sample size in prevalence study.

$$n = \frac{z^2 \cdot p(1-p)}{d^2}$$

Where $n$ is the sample size, $Z$ is the statistic corresponding to level of confidence, $P$ is expected prevalence (that can be obtained from same studies or a pilot study conducted by the researchers), and $d$ is precision (corresponding to effect size).
The level of confidence usually aimed for is 95%, most researchers present their results with a 95% confidence interval (CI). However, some researchers wants to be more confident can chose a 99% confidence interval. Researcher needs to know the assumed P in order to use in formula. This can be estimated from previous studies published in the study domain or conduct a pilot study with small sample to estimate the assumed P value.

Sample size calculation in case control study

The case-control is a type of epidemiological observational study. It is often used to identify risk factors that may associated to a disease by comparing the risk factors in subjects who have that disease (the cases) with subjects who do not have the disease (the controls).

The sample size calculation for unmatched case control studies (the number of cases and controls) needs these assumptions; the assumed number of cases and controls who experienced the risk factors from similar studies or from a pilot study (also researchers can use the assumed odds ratio; OR), the level of confidence (almost 95%) and the proposed power of the study (would be from 80%). There are software or guide books that provide the investigators with the formula or the sample size calculated in tables according to different assumptions. But researchers should remember that, in the presence of a significant confounding factor, researchers require a larger sample size. Since the confounding variables must be controlled for in any analysis, a more complex statistical model must be made, so a larger sample is required to achieve significance.

Sample size calculation in clinical trials

In a clinical trial, if the sample size is too small, a well conducted study may fail to answer its research hypothesis or may fail to detect important effects and associations. The minimum information needed to calculate sample size for a randomized controlled trial includes the power, the level of significance, the underlying event rate in the population and the size of the treatment effect sought. Besides this, the calculated sample size should be adjusted for other factors including expected compliance rates and, less commonly, an unequal allocation ratio.

In conclusion, sample size calculation is a very important aspect of any study. It should be done at the time of planning a study, based on the type of the research question and study design. It is advisable to take the help of a statistician at this stage of the study as well. Authors must provide detailed information regarding the sample size calculation used when publishing their papers.

References:
Tranexamic acid in Obstetrics and Gynaecology

Dr. Charmila Ayyavoo MD DGO DFP PGDCR
Chairperson, Clinical Research Committee, FOGSI
2016-18
Director, Aditi Hospital & Parvathy Ayyavoo Fertility Centre, Trichy

Background:
Tranexamic acid is an anti-fibrinolytic agent. Research was undertaken by a husband and wife team in Japan in the 1950s for a drug to reduce maternal mortality due to postpartum haemorrhage. The team was Shosuke and Utako Okamato from Keio and Kobe Medical schools. The research was started on epsilon amino caproic acid [EACA] which is an anti fibrinolytic agent. They invented in 1962, 1-(amino methyl)-cyclohexane-4-carboxylic acid (AMCHA) also called tranexamic acid. It is 27 times more potent than EACA.[1]

Pharmacokinetics:
Tranexamic acid is a synthetic analogue of lysine, an amino acid. Oral route or a short intravenous infusion of the drug is the mode of usage. It will attain peak activity instantly and is eliminated in urine within three hours. The drug prevents bleeding episodes by inhibiting the enzymatic breakdown of fibrin blood clots. It reduces the binding of plasminogen and tissue plasminogen activator to fibrin. [2]

Trials based on the usage of tranexamic acid:
The CRASH-2 (Clinical Randomization of Antifibrinolytic in Significant Hemorrhage) trial was initiated in 2005. It was a large multicenter randomized trial of the effect of tranexamic acid on death and vascular occlusive events in patients with bleeding trauma. The results were published in 2010. A total of 20,211 adult patients with trauma along with significant bleeding, who were within 8 hours of their injury, were randomly allocated to receive tranexamic acid (1 gram over 10 minutes, followed by an infusion of 1 gm over 8 hours) or matched placebo. The primary outcome was death in hospital within 4 weeks. Tranexamic acid significantly reduced death due to bleeding and all-cause mortality with no increase in vascular occlusive events. The reduction in death due to bleeding was greatest when tranexamic acid was given within 3 hours of injury. When it was given beyond 3 hours of the injury, there was no mortality benefit, and some suggest an increased risk of bleeding, possibly a manifestation of thrombotic disseminated intravascular coagulation. [3]

World Health Organization [WHO]: [4,5]
On the basis of the results of the CRASH-2 trial, tranexamic acid was included on the World Health Organization's (WHO) List of Essential Medicines and was also incorporated into trauma protocols in many countries around the world.
WOMAN trial 2009 [6]
 Whilst the CRASH-2 trial was still underway, the WOMAN (World Maternal Antifibrinolytic) trial was launched in 2009, with an aim to provide robust, definitive evidence on the use of tranexamic acid in post-partum hemorrhage. The results of this multicenter, randomized, double-blind, placebo-controlled trial of the effect of tranexamic acid on death or hysterectomy in women with post-partum hemorrhage were published in 2017. Tranexamic acid significantly reduced death due to bleeding with no increase in thromboembolic events or complications. The effect on death due to bleeding was greatest when tranexamic acid was given within 3 hours of childbirth. When it was given beyond 3 hours of childbirth, there was no apparent reduction in death due to bleeding.

TRAAP trial: Tranexamic Acid for Preventing Postpartum Hemorrhage Following a Vaginal Delivery trial [7]
 It is a multicenter, placebo controlled, double-blind trial that randomized 4079 women to receive either tranexamic acid or placebo. There was no reduction in post-partum hemorrhage when it is used as a prophylaxis before a vaginal delivery. It shows a 25% reduction in clinically significant postpartum hemorrhage after a vaginal delivery.

Protocol for the usage: [8]
The WHO strongly recommends early treatment of PPH (within 3 hours of birth) with intravenous [IV] tranexamic acid using the same dosing regimen as that used in the WOMAN trial. A fixed dose of 1 g in 10 mL (100 mg/mL) is given intravenously at a rate of 1 mL per minute. A second 1 g IV should be administered if bleeding continues after 30 min or restarts within 24 hours of the first dose.

Method of administration:
It can be mixed with electrolyte solutions, carbohydrate solutions, amino acid solutions and dextran solutions. It should not be mixed with blood for transfusion or solutions containing mannitol or penicillin.

Contraindications to anti-fibrinolytic therapy are
• known thromboembolic event during pregnancy
• known hypersensitivity to tranexamic acid
• active intravascular clotting or
• a history of coagulopathy
**Indications in obstetrics:** [9]

Tranexamic acid should be given to all women with ‘clinically estimated blood loss of

- more than 500 mL after vaginal birth or
- 1000 mL after caesarean section, or
- any blood loss that is sufficient to compromise hemodynamic stability regardless of the cause of hemorrhage.

It should be used in addition to all usual treatments for the management of PPH including medical (uterotonics), non-surgical and surgical interventions.

Intramuscular tranexamic acid can be given if there is no facility to give intravenous infusion as in low resource settings before shifting to higher centers. In healthy volunteers, intramuscular tranexamic acid achieves therapeutic levels (>10 mg/L) at approximately 30 minutes. Health workers can be trained to give intramuscular oxytocin but the ideal route is the intravenous route. [8]

In a study by Simran et al, the use of tranexamic acid in cesarean delivery has been studied in India. In the study group of 50 patients, tranexamic acid 1 gm IV was given 20 minutes before making incision for caesarean section and the control group of 50 did not receive tranexamic acid. The study concludes that a safe dose of tranexamic acid has an effective role in reducing blood loss during LSCS without causing adverse reaction. [10]

**Usage in threatened miscarriage:**

Bleedings in the first and second trimesters of pregnancy with chorionic/placental abruption can be treated with tranexemic acid. It allows to achieve a rapid normalization of hemostasis, promoting successful prolongation of pregnancy.[11] It has rapid and effective action on sub chorionic hematoma in the absence of embryotoxic and coagulopathy influence. In the first trimester, tranexamic acid does not cause any significant disorders of hemostatic system. According to a study by Heryak et al, a complex application of natural micronized progesterone 100 mg three times a day sublingually and 500 mg of Tranexamic acid dissolved in 200 ml normal saline helped in prolonging pregnancies. [12]

**Usage in Gynaecology:**

The drug is an effective treatment to reduce the volume of bleeding during menstruation. It is found to be superior to both placebo and oral progestins, and as good as combined oral contraceptives at reducing menstrual blood volume. It is known to reduce the volume of bleeding during abdominal myomectomy as well as hysterectomy.[13]

It has been tried during hysterectomy, myomectomy, cervical conization, hysteroscopy, and surgery for cervical and ovarian cancer. Tranexemic acid [TXA] is a safe adjunct that can be considered in a variety of gynecologic surgeries to decrease blood loss and risk of blood transfusion. [14]
Intrauterine Instillation of Tranexamic Acid in Hysteroscopic Myomectomy:
One gram of TXA for every 1000 mL of the distending medium is instilled. There is a statistically significant decrease in hemoglobin level 24 hours after surgery, albeit with minimal clinical significance. TXA results in better visualization of the field throughout the procedure. [15]

Menorrhagia induced by intrauterine device [IUD]:
A Comparative Trial of the Efficacy of Mefenamic Acid and Tranexamic Acid for Treatment of Menorrhagia Induced by Copper T-380A IUD:
A dose of 500 mg three times daily for 3-5 days of three menstrual cycles is given. The study concludes that tranexamic acid and mefenamic acid have the same significant effect in reducing mean blood loss volume and duration of menstruation in TCu380A IUD users. [16]

Conclusion:
Tranexemic acid is a drug which can be added to the armamentarium of drugs used in the prophylaxis and therapy of hemorrhage in obstetrics and gynecology. If used at the apt time, it can contribute considerably to a reduction in morbidity and mortality in women.

References:
• Role of tranexamic acid in reducing blood loss during and after caesarean section Simran Kaur Bhatia, Hemant Deshpande Department of Obstetrics and Gynaecology, Padmashree Dr. D. Y. Patil Medical College Hospital and Research Centre, Pune, Maharashtra, India
• Klebanoff et al: Applications of Tranexamic acid in benign gynecology, Current Opinion in Obstetrics and Gynecology: August 2019 - Volume 31 - Issue 4 - p 235-239
Glimpses
Comprehensive update on stillbirth

Asthा Srivastava*,  A. G. Radhika**
*Assistant professor, **Senior Consultant,
Department of Obstetrics & Gynaecology,
UCMS&GTB Hospital, Delhi

Introduction
World Health Organization defines stillbirth as a baby born with absolutely no signs of life at or after 28 weeks gestation, weight ≥ 1000 g, crown-heel length (CHL) ≥ 35 cm. Annually, an estimated 2.6 million stillbirths occur worldwide. About 98% of all stillbirths occur in low- and middle-income countries with three quarters in sub-Saharan Africa and south Asia. [1].

As per the national HMIS 3,03,857 stillbirths were reported for the year 2015-16 (neonatal deaths at 22/1000 live births [2]). In 2014, the World Health Assembly endorsed a target of 12 or fewer stillbirths per 1000 births in every country by 2030. The Government of India has developed an Indian Newborn Action Plan which includes efforts to reduce stillbirths to <10 per 1000 births by 2030 [3]

Classification:
There are over 100 classification systems for perinatal mortality. Classification systems incorporating the use of specific diagnoses such as those listed in the International Classification of Disease (ICD) have also been used. However, many specific diagnoses relating to perinatal death are missing from even the most recent ICD classification. A more recent classification system considers the Relevant Condition at Death (ReCoDe). ReCoDe acknowledges conditions associated with death, instead of solely reporting causative disorders, and reduces the number of previously classified “unexplained” deaths from 40% to 15%.

Risk Factors associated with still birth:
1. **Race**: Non-Hispanic black women have more than twice stillbirth rate than other racial groups (10.53 deaths per 1,000 livebirths and stillbirths) (4).
2. **Younger and Older Maternal Age**: Maternal age less than 15 years and greater than 35 years is an independent risk factor for stillbirth. Maternal age greater than or equal to 35 years of age is associated with an increased risk of stillbirth in nulliparous and multiparous women (5).
3. **Multiple Gestations**: The stillbirth rate is approximately 2.5 times higher in twin pregnancies than in singleton gestation (14.07 versus 5.65 per 1,000 live births and stillbirths) (4). The risk of stillbirth increases in all twins with advancing gestational age, and it is significantly greater in monochorionic as compared with dichorionic twins (6).
4. Past Obstetric History:
Women with a previous stillbirth are at increased risk of recurrence. Compared with women with no history of stillbirth, women who had a stillbirth in an index pregnancy had an increased risk in subsequent pregnancies (pooled odds ratio, 4.83; 95% CI, 3.77–6.18), which remained significant after adjustment for confounding factors (7). Women with previous adverse pregnancy outcomes, such as preterm delivery, growth restriction, or pre-eclampsia, are at increased risk of stillbirth in subsequent pregnancies (8).

5. Comorbid Medical Conditions:
Many maternal medical conditions are associated with an increased risk of stillbirth (Table 1).

6. Acquired and Inherited Thrombophilias:
Antiphospholipid syndrome (APS) is an acquired thrombophilia that is associated with stillbirth. In contrast, inherited thrombophilias have not been associated with stillbirth, and testing for them as part of a stillbirth evaluation is not recommended (9).

7. Substance Use:
Maternal cocaine, methamphetamine, other illicit drug use, and smoking tobacco, are all significant contributors to abruption and stillbirth.

8. Assisted Reproductive Technology:
Pregnancies achieved by in vitro fertilization (IVF) appear to be associated with an elevated risk (twofold to threefold increase) of stillbirth even after controlling for age, parity, and multifetal gestations (10).

Potential Causes of Stillbirth:
Approximately 25 to 60 percent of fetal deaths remain unexplained [11]. In the remaining stillbirths causes can be divided into maternal, fetal or placental.

<table>
<thead>
<tr>
<th>Maternal causes</th>
<th>Fetal causes</th>
<th>Placental causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>Birth defects or genetic problems</td>
<td>Abruption</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Small for gestational age</td>
<td>Chorioamnionitis</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Infection</td>
<td>Vasa previa</td>
</tr>
<tr>
<td>Intrahepatic cholestasis of pregnancy</td>
<td>an unrecognized arrhythmia such as prolonged QT syndrome</td>
<td>Umbilical cord accidents such as cord prolapse, occlusion, entanglement</td>
</tr>
<tr>
<td>Anti phospholipid antibody syndrome</td>
<td>Hydrops fetalis</td>
<td>Prolonged pregnancy</td>
</tr>
<tr>
<td>Feto maternal haemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoimmune disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Maternal or fetal infections are associated with about 10–25% of stillbirths in high-income countries and approximately 50% of stillbirths in low-income and middle-income countries [12].

Infection can cause stillbirth by several mechanisms.

- Severe maternal illness: Maternal infection might lead to mother becoming severely ill (eg, severe influenza), and the fetus might die because of high maternal fever, respiratory distress, or other systemic reactions, without organisms transmitted to the placenta or fetus.
- Placental infection that prevents oxygen/nutrients from crossing to fetus (eg malaria)
- Fetal infection that causes lethal congenital deformity or damages a vital organ
- Precipitation of preterm labor, with intrapartum fetal death.

Bacterial infections leading to stillbirth can be divided into:

**Transplacental:** That reach the fetal compartment through the placenta (Listeria monocytogenes or syphilis). In transplacental infections (e.g., syphilis), the placental villi often show evidence of infection and liver is most frequently infected as the organisms enter the fetus through the umbilical vein.

**Ascending infection:** That ascend from the vagina through the cervix (eg, group B streptococcus or Escherichia coli). Organisms that ascend from the vagina into the uterus enter the amniotic fluid either through intact choriodecidual membranes or after membrane rupture. The most common organ infected is the fetal lung, associated with fetal breathing of contaminated amniotic fluid. Consequently, a common autopsy finding in stillbirths is pneumonitis.

Viral infections associated with stillbirth include cytomegalovirus, parvovirus, and Zika. Serology for toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus is not recommended as it is of unproven benefit (13).

**Clinical Considerations and Management**

Management of stillbirth is based on gestational age, suspected etiology, maternal history of previous uterine scars, and maternal wishes. Care should be individualized and involve the woman and her family in the decision-making process.

Between 80% and 90% of women will spontaneously labor within 1–2 weeks of diagnosis of the stillbirth.

In rare cases, when the latency period is prolonged beyond 4 weeks, retention of a stillbirth may lead to a chronic consumptive coagulopathy due to gradual release of tissue factor from the decidua or placenta into the maternal circulation. Coagulation abnormalities occur in about 3–4% of patients with uncomplicated in utero demise of > 24 weeks with expectant management lasting for more than 3 weeks and is increased in the presence of placental abruption [14].

**Maternal Evaluation:**

A thorough maternal history should be taken to look for known conditions or symptoms suggestive of those that have been associated with stillbirth. History should focus on following aspects [15].
Current pregnancy
- Maternal age
- Gestational age at stillbirth
- Pregnancy weight gain and body mass index
- Medical conditions complicating pregnancy (Cholestasis, hypertensive disorder of pregnancy, diabetes in pregnancy)
- Complications of multifetal gestation, such as twin–twin transfusion syndrome, twin reversed arterial perfusion syndrome, and discordant growth
- Placental abruption
- Abdominal trauma
- Preterm labor or rupture of membranes
- Abnormalities seen on ultrasound
- Infection or chorioamnionitis
- Previous fetal demise or previous child with anomaly or growth restriction
- Previous history of placental abruption

Past Maternal history
- Diabetes mellitus
- Chronic hypertension
- Previous venous thromboembolism
- Thrombophilia
- Systemic lupus erythematosus
- Autoimmune disease
- Epilepsy
- Severe anaemia
- Heart disease
- Tobacco, alcohol, drug or medication use

Maternal laboratory evaluation
- Complete blood count (CBC): to look for any evidence of maternal disorder like infection as the cause of fetal death.
- Glucose screening (oral glucose tolerance test, hemoglobin A1C)
- Indirect Coombs test to exclude red cell alloimmunization.
- Serologic testing for syphilis if not done earlier in pregnancy.
- Fetal–maternal hemorrhage screen: Kleihauer-Betke test or flow cytometry to look for fetal cells in maternal circulation- detection of large feto maternal hemorrhage may explain an otherwise unexplained still birth [16].
- Fetal–maternal hemorrhage is suspected as a part of the pathophysiologic process in 1–13% of stillbirths.
- Thyroid and liver function tests if there is a clinical suspicion (eg, maternal signs/symptoms) or to evaluate unexplained stillbirth.
- Lupus anticoagulant and anticardiolipin and anti-beta2-GP I antibody titers (immunoglobulin M [IgM] and IgG) to exclude antiphospholipid syndrome, especially in the presence of growth restriction or severe preeclampsia [15].
- Routine testing for inherited thrombophilias is not recommended [15]
Clinical history, placental histology and autopsy should be performed whenever possible. If infection is suspected based on findings from the history or fetal and placental evaluation, then testing for specific infections in maternal, fetal or placental tissues may be appropriate.

Toxicology screen: In cases of placental abruption or when drug abuse is suspected

Examination of Placenta & Cord:
Gross and microscopic examination of the placenta, umbilical cord, and fetal membranes is an essential component of the evaluation. Gross evaluation may reveal conditions such as

- Hematoma, infarcts.
- Calcification: Calcium deposits are commonly observed on the maternal surface of normal term placentas and are considered a normal part of placental aging. They are of no clinical significance if seen in a term placenta. Calcium speckling identified in a placenta from a fetus at less than 32 weeks’ gestation, however, has been associated with low birth weight, low Apgar scores, and neonatal death.
- Infection: Greenish yellow membranes or adherent purulent material or foul odour may indicate chorioamnionitis
- Amnion nodosa are white-yellow, 1- to 2-mm nodules that can be easily removed from the fetal membranes. These nodules can be identified in the examination of a placenta in which the pregnancy was complicated by marked oligohydramnios [17]. The amnion is maintained by amniotic fluid; therefore, in the absence of amniotic fluid, the amnion degenerates. Amnion nodosa represent the precipitation of vernix caseosa and are composed of desquamated fetal epithelial cells, fibrin, and hair.
- Umbilical cord knots or tangling should be noted but interpreted with caution, as cord entanglement occurs in approximately 25% of normal pregnancy [15].

Aerobic and anaerobic bacterial cultures should be performed on the placenta, especially if autopsy is declined.

Examination of the Stillborn Fetus:
The general examination of the stillborn fetus should be done promptly to note the following

- Body weight
- Crown-to-rump length (crown to ischial tuberosities, "sitting height")
- Crown-to-heel length (crown to heel of extended leg)
- Head circumference
- Foot length (especially useful before 23 wks of gestation to ascertain gestational age)
- Photographs of the whole body (unclothed); frontal and profile views of the face, extremities, and palms; and close-up photographs of specific abnormalities

Fetal autopsy should be offered because it is one of the most useful diagnostic tests in determining the cause of death. If parents do not give consent for complete autopsy, other options depending upon parent’s consent include gross visual external examination or postmortem imaging studies only, restrictions to specific organs/regions.
Postmortem imaging studies:
Radiography is particularly helpful when skeletal malformations are suspected and it is the single most important diagnostic test for many skeletal dysplasias. It can exclude most skeletal abnormalities without the need for autopsy.

MRI has good spatial resolution and excellent soft tissue contrast, and it is potentially useful for imaging the brain and musculoskeletal system when autopsy is declined [18]. In addition, the advent of MRI fluoroscopy and MRI guided biopsy makes it possible to obtain targeted biopsy specimens of specific tissues [19]. However, MRI has so far proven of limited value for assessing anomalies of the cardiovascular system and does not provide the same level of diagnostic information as an autopsy.

Fetal postmortem computed tomography (CT) scan has excellent diagnostic value for musculoskeletal abnormalities [20]. However, without contrast, it yields a low success rate for the examination of the brain and thoracoabdominal organs compared to MRI[20]. Whole-body fetal postmortem CT angiography is feasible and may have value in the diagnosis of complex cardiac malformations after intracardiac injection of contrast, but the diagnostic accuracy of this method is yet to be confirmed.

For fetuses beyond 20 weeks, MRI is preferred over USG and CT[20].

The disadvantage of using imaging techniques for stillbirth investigations is the lack of histologic, material for analysis, and therefore possibly lower level of diagnostic information obtained [18].

When a full autopsy is performed, it should follow published guidelines and protocols for perinatal autopsy [21]. These include measurements to establish gestational age (foot length and body weight), estimation of interval between death and delivery, identification of intrinsic abnormalities and developmental disorders, and investigation for evidence of infection

Fetal genetics evaluation:
The American College of Obstetricians and Gynecologists (ACOG) recommends genetic evaluation of all stillbirths after appropriate parental consent [15]. Chromosomal microarray is preferred over conventional karyotype analysis to provide a genetic diagnosis. Karyotype or microarray are of higher yield if the fetus displays dysmorphic features, inconsistent growth measurements, anomalies, hydrops, or growth restriction [22].

Acceptable cytogenetic specimens include:
• Amniotic fluid: Amniocentesis for fetal karyotyping has the highest yield and is particularly valuable if delivery is not expected imminently [23].
• Placental block taken from below the cord insertion site that includes the chorionic plate and an umbilical cord segment.
• An internal fetal tissue specimen that thrives under low-oxygen tension such as costochondral or patellar tissue. It is to be noted that fetal skin is sub-optimal [15].

Support services and clinical counseling
Patient support should include emotional support and clear communication of test results. Communication with bereaved parents should be clear and honest.
Care in a subsequent pregnancy:
Compared with women whose first infant was live born, those with a previous stillborn infant are 2.5 times (95% CI, 1.4–4.7) more likely to have a subsequent stillbirth (24). The risk of recurrent still-birth may be increased as high as 10-fold depending on maternal race and characteristics of the previous stillbirth, such as etiology, gestational age, and presence of fetal growth restriction (25).

• Pre pregnancy or Initial Prenatal Visit
  • Detailed medical and obstetric history.
  • Evaluation and workup of previous stillbirth
  • Determination of recurrence risk
  • Smoking cessation
  • Weight loss in obese women (prepregnancy only)
  • Genetic counseling if applicable
  • Diabetes screen
  • Acquired thrombophilia testing: lupus anticoagulant as well as IgG and IgM for both anticardiolipin and b2-glycoprotein antibodies
  • Support and reassurance

First Trimester
  • Dating ultrasonography
  • First-trimester screen: pregnancy-associated plasma protein A, human chorionic gonadotropin, and nuchal translucency* or cell-free fetal DNA testing
  • Support and reassurance

Second Trimester
  • Fetal sonographic anatomic survey at 18–20 weeks
  • Offer genetic screening if not performed in the first trimester
  • Support and reassurance

Third Trimester
  • Sonographic screening for fetal growth restriction after 28 weeks

Antepartum fetal surveillance:
For patients with a previous stillbirth at or after 32 0/7 weeks, once or twice weekly antenatal surveillance is recommended at 32 0/7 weeks or starting at 1–2 weeks before the gestational age of the previous stillbirth. For stillbirth that occurred before 32 0/7 weeks of gestation, individualized timing of antenatal surveillance should be planned.

Specific pharmacological treatments:
Pharmacological interventions may be directed at optimizing maternal health or reducing the risk from placental disorders. These include
1. Tab Aspirin: 150 mg once at night, ideally commenced before 16 weeks of gestation and continued until at least 36 weeks
2. Low-molecular-weight heparin (LMWH)
There is currently no high-grade evidence to support the use of low-molecular-weight heparin (LMWH) with the primary aim to prevent fetal complications in women with a history of stillbirth. However, it should be used in women at high risk of maternal venous-thromboembolism or anti phospholipid syndrome.

**Delivery**

Planned delivery at 39 weeks of gestation is recommended or as dictated by other maternal or fetal comorbid conditions.

**Maceration: prediction of timing of death**

Skin peeling and maceration known to start at about 8-12 hours. Maceration may not be a precise predictor of timing of death. High microbial load in the amniotic fluid, prolonged hypoxia prior to actual death, and maternal fever may result in more maceration. Autolytic changes may accelerated with increased temperature as in maternal hyperthermia/sepsis associated with prolonged rupture of membranes, chorioamnionitis. Of 201 fetuses moving when labor started, 24% were found macerated and of 117 fetuses not moving when labor started, 34% were described as fresh. Therefore caution needs to be exercised when using fetal appearance as indicator of intrapartum death [26].

**Table 2:**[15]

Estimated rate of still birth with maternal or fetal condition

<table>
<thead>
<tr>
<th>condition</th>
<th>Estimated rate of still birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>All pregnancies</td>
<td>6.4/1000</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>• Treated with diet (A1)</td>
<td></td>
</tr>
<tr>
<td>• Treated with insulin</td>
<td>6–10/1000</td>
</tr>
<tr>
<td></td>
<td>6–35/1000</td>
</tr>
<tr>
<td>Hypertensive disorder</td>
<td></td>
</tr>
<tr>
<td>• Chronic hypertension</td>
<td>6–25/1000</td>
</tr>
<tr>
<td>• Preeclampsia</td>
<td>9–51/1000</td>
</tr>
<tr>
<td></td>
<td>12–29/1000</td>
</tr>
<tr>
<td></td>
<td>without severe features</td>
</tr>
<tr>
<td></td>
<td>with severe features</td>
</tr>
<tr>
<td>Growth restricted fetus</td>
<td>10–47/1000</td>
</tr>
<tr>
<td>Multiple Gestation</td>
<td></td>
</tr>
<tr>
<td>• Twins</td>
<td>12/1000</td>
</tr>
<tr>
<td>• triplets</td>
<td>34/1000</td>
</tr>
<tr>
<td>oligohydramnios</td>
<td>14/1000</td>
</tr>
<tr>
<td>Late term pregnancy (greater than 41 weeks)</td>
<td>14-40/1000</td>
</tr>
<tr>
<td>Medical Condition</td>
<td>Incidence Rate</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Previous stillbirth</td>
<td>9–20/1000</td>
</tr>
<tr>
<td>Decreased fetal movement</td>
<td>13/1000</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>40–150/1000</td>
</tr>
<tr>
<td>Renal disease</td>
<td>15–200/1000</td>
</tr>
<tr>
<td>Cholestasis of pregnancy</td>
<td>12–30/1000</td>
</tr>
<tr>
<td>Advanced maternal age</td>
<td>11–14/1000</td>
</tr>
<tr>
<td>• 35–39 years</td>
<td>11–21/1000</td>
</tr>
<tr>
<td>• 40 years or greater</td>
<td></td>
</tr>
<tr>
<td>Black maternal race</td>
<td>12–14/1000</td>
</tr>
<tr>
<td>Maternal age &lt; 20 years</td>
<td>7–13/1000</td>
</tr>
<tr>
<td>Assisted reproductive technology</td>
<td>12/1000</td>
</tr>
<tr>
<td>Obesity (prepregnancy BMI equal to or greater than 30 kg/m²)</td>
<td>13–18/1000</td>
</tr>
<tr>
<td>Smoking greater than 10 cigarettes per day</td>
<td>10–15/1000</td>
</tr>
</tbody>
</table>

Table 3 placental examination checklist:

<table>
<thead>
<tr>
<th>SIZE</th>
<th>Diameter (cm): 15 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg): 450gm-650 gm (normal wt)</td>
<td>Accessory lobes (yes/no)</td>
</tr>
<tr>
<td>Structure</td>
<td>Fetal surface (hemangioma)</td>
</tr>
<tr>
<td>Intact (yes/no)</td>
<td>Lesions (amnion nodosa, bands)</td>
</tr>
<tr>
<td>Lesions</td>
<td>Umbilical Cord Structure</td>
</tr>
<tr>
<td>Maternal surface (calcifications, hematoma, infarct)</td>
<td>Number of vessels: 3 (normal)</td>
</tr>
<tr>
<td>Amnion</td>
<td>Length (cm): 37 cm</td>
</tr>
<tr>
<td>Color</td>
<td>Coiling (normal, hypo-, hyper-)</td>
</tr>
<tr>
<td>Umbilical Cord Structure</td>
<td>Continuity (knots, torsion)</td>
</tr>
<tr>
<td>Insertion site</td>
<td>Multiple Gestation</td>
</tr>
<tr>
<td>Central, velamentous, marginal, furcate</td>
<td>Chorionicity</td>
</tr>
<tr>
<td>Amnionicity</td>
<td></td>
</tr>
</tbody>
</table>
References


Quiz on Research Methodology

Q-1 Who is regarded as father of scientific social survey
A. Best  
B. Darwin  
C. Booth  
D. None of these

Q-2 To pursue research which of the following is the first requirement
A. Developing a research design  
B. Formulating a research question  
C. Deciding about the data analysis procedure  
D. Formulating a research hypothesis

Q-3) In which of the following study Relative risk can be calculated
A. Cohort study  
B. Case control study  
C. Longitudinal study  
D. Cross section study

Q-4) The core requirement of a dissertation are
A. Introduction, data collection, data analysis, conclusions and recommendations  
B. Executive summary, literature review, data collection, conclusions, bibliography  
C. Introduction, literature review, research methods, results, discussion, conclusions  
D. Research plan, Research data, Analysis and reference

Q-5____________________is the preferred sampling method for a population with finite size

Q-6) What is the name of conceptual framework in which the research is carried?
A. Research hypothesis  
b. Research synopsis  
c. Research paradigm  
d. Research design
Q-7) How is random sampling helpful?
A. Reasonably accurate
B. Free from personal biases
C. An economical method
D. All of the above

Q-8) A measurable attribute that varies across study unit is known as
A. Intervention
B. Variable
C. Correlation
D. Exposure

Q-9) All are example of descriptive studies except
A. Cross sectional survey
B. Case series
C. RCT
D. Case report

Q-10) Which one is called non-probability sampling?
A. Quota sampling
B. cluster sampling
C. Systemic sampling
D. stratified Random sampling

Answers:
1-C
2-B
3-A
4-C
5-Systematic sampling
6- D
7-D
8-B
9-C
10- A
Thalassemia: It is the disorder of haemoglobin which is inherited in autosomal recessive pattern. Hence, a diagnosis of thalassemia major in a child indicates that both its parents are carrier of thalassemia. Carrier screening and prenatal diagnosis is possible and can prevent birth of an affected child in a family. As an obstetrician, each one of us have an obligation for predicting and diagnosing the condition. This chapter is written to explain the genetic basis of this disease.

Haemoglobin: The adult haemoglobin(Hb) is HbA, consist of two alpha (α) and two beta (β)globin chains, represented as α2β2, each linked to a heme molecule[1]. Other minor hemoglobins in adults are HbF- fetal haemoglobin(α2γ2) and HbA2(α2δ2).

- Major Adult Hb(Hb A): α2β2 -96 to 97%
- Hb A2 : α 2δ2 - 2.5 to 3.5%
- Fetal Hb (Hb F): (α 2γ2)- <1%

Types of hemoglobinopathies:
The hemoglobinopathies are of two types:

- *Thalassemias* - decreased globin chain production
- *Hemoglobin structural variants* - change in structure of β globin chain (eg, Hb S, Hb C, Hb E, Hb D Punjab)

A normal individual has four α globin genes on short arm of chromosome 16 (two gene per chromosome(αα/αα)) and two β globin genes on short arm of chromosome 11 (β/β). The γ and δ genes are also on chromosome 11. Genetic alterations in one or more of different globin genes leads to hemoglobinopathies.

Rationale for hemoglobinopathy screening:
Thalassemias and hemoglobin structural variants are autosomal recessive disorders. Thus couple who are heterozygote carriers of gene mutation have a 25 percent chance of having an offspring with a hemoglobinopathy. The purpose of prenatal hemoglobinopathy screening is to identify and counsel asymptomatic individuals whose offspring are at risk of an inherited hemoglobinopathy[2]. Hemoglobinopathy carrier screening should be offered to all pregnant women as carrier frequency is common in Indian population. If screening is not done before pregnancy, it should be performed early in pregnancy so that fetal diagnosis, if indicated, can be performed when parents have the option of terminating the pregnancy.
Prenatal diagnosis of fetal hemoglobinopathy is offered by chorionic villus sampling (10-14 weeks) or amniocentesis (after 15 weeks) when the couple is found to be carrier.

**Thalassemia**
Most common inherited single-gene disorder due to reduced alpha or beta globin chain synthesis leading to imbalance in ratio of alpha to beta chains[3].

Types of thalassemia:
- **Beta Thalassemia**: synthesis of β globin chain is decreased or absent.
- **Alpha Thalassemia**: synthesis of α globin chain is decreased or absent

Point mutations are the most common causes of beta thalassemia, while deletion of one or more of the four alleles (αα /αα) present in a normal diploid erythroid progenitor is the most common cause of alpha thalassemia. This abnormal alpha- to beta-chain ratio causes the unpaired chains to precipitate and causes destruction of red blood cell precursors in the bone marrow (ineffective erythropoiesis) and circulation (haemolysis). As a result, affected individuals have variable degree of anaemia and extramedullary haematopoiesis. This causes impaired growth, bone changes and iron overload.

**Beta Thalassemia**: Mutation in beta globin gene leads to decreased (β+) or absent (β0) beta globin chain production. The carrier rate is high in the country and is estimated to be 3%. In some states like Maharashtra, Punjab it can be as high as 10%. The severity of disease correlates with the amount of normal beta globin production. Beta globin expression begins during infancy as alpha and gamma globin is used in fetal haemoglobin (HbF). Thalassemia phenotype generally begins to manifest during the first year of life and typical age of presentation is four to six months.

**Beta thalassemia trait or beta thalassemia minor** - These are heterozygotes (β/β0, β/β+) and are carrier. Complete blood count will show mild or no anaemia, and low mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH). Reduced production of beta globin chain causes decrease in normal HbA (α2β2). They compensate by increasing production of δ and γ chains, leading to increases in the levels of minor hemoglobins HbA2 (α2δ2) and HbF (α2γ2)[4]. Hb electrophoresis or high performance liquid chromatography (HPLC) will demonstrate increases in HbA2 (> 3.5%) and HbF (>1%) [5]. If the woman is found to be carrier partner is tested for carrier status.

**Beta thalassemia intermedia/ beta thalassemia major** - Two mutated beta globin genes are inherited, one from each parent. In intermedia there is limited β globin production (β+/β+ or β+/β0). In major there is no β globin chain synthesis (β0/β0). The clinical distinction between intermedia and major is made by degree of transfusion support that is required.[4] Intermedia patients require periodic transfusion, while in beta thalassemia major, regular lifelong blood transfusions are required. Prolonged transfusion therapy results in iron overload with resultant toxicity over heart, liver and other body organs.
There are more than 200 different β chain mutations. Few mutations are responsible for most of the disease causing alleles in different part of world .This facilitate molecular genetic testing. Most common mutation in India include −619 bp deletion, cd 8/9 + G, IVS1-1 G→T, IVS1-5 G→C, 41/42-TTCT which account for 90-95% of cases. Once the carrier status of couple is confirmed, next step is to characterize their DNA mutation. Prenatal invasive testing is offered to extract fetal DNA and the same mutation is looked in the fetus.

**Alpha Thalassemia**-Deficiency/Absence of α globin chain. Four copies of genes are responsible for synthesis of α globin chains(αα /αα). The different types of α-thalassemia is due to deletional mutations involving α globin gene .Presentation depend on number of genes deleted.

**Table 1 Presentation of Alpha thalassemia**

<table>
<thead>
<tr>
<th>Type</th>
<th>Genotype</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>αα/αα</td>
<td></td>
</tr>
<tr>
<td>Silent carrier</td>
<td>αα/α-</td>
<td>Asymptomatic, MCV and/or MCH can be low. Diagnosis of single gene deletion by molecular (DNA) testing.</td>
</tr>
<tr>
<td>α-thalassemia trait</td>
<td>α0 : αα/-α+ α+ : α-/α-</td>
<td>Mild anaemia, microcytosis, hypochromia .Peripheral blood smear shows H bodies(not 100% sensitive) . Diagnosis is by molecular methods.</td>
</tr>
<tr>
<td>Hb H disease</td>
<td>α-/-</td>
<td>clinically mild anaemia, microcytosis, hypochromia. Many patients require occasional transfusion</td>
</tr>
<tr>
<td>Hb Bart’s disease</td>
<td>--/--</td>
<td>Presents as severe fetal anaemia(Hydrops fetalis)</td>
</tr>
</tbody>
</table>

When both parents are carrier of α 0- thalassemia(α α /--),couple has 25% risk of having fetus with all four α globin genes deleted (Hb Bart’s disease --/--). In that case there will be no α globin chain production. Fetus is thus unable to make HbF or HbA and presents as hydrops fetalis[6].Diagnosis is done by molecular studies to see gene deletion.

**Variant haemoglobins** -It occurs due to mutation that results in production of a mutant (“variant”) beta globin chain. It includes haemoglobin S, C,E, D Punjab.Sickle cell anaemia is the most common variant.

**Hemoglobin S**: There is substitution of valine for glutamic acid in sixth amino acid position of β globin chain.

Sickle cell trait-Heterozygotes (HbAS)-They have no clinical symptoms and have normal life span.

Sickle cell disease-Homozygotes (HbSS). HbS mutation in beta globin gene is inherited from both parents. RBCs assume sickle shape in low oxygen tension. It presents as chronic haemolytic anaemia, heightened susceptibility to infection, end-organ damage and intermittent attacks of vascular occlusion causing acute and chronic pain. HPLC is suggestive of primarily HbS (with small amounts of HbA2 and HbF)
Hemoglobin E- There is substitution of lysine for glutamic acid at 26th position of the β globin chain. Homozygotes for HbE have severe disease with profound anemia.

Hemoglobin C- Glutamic acid in 6th position of β-chain is replaced by lysine. The heterozygous form (HbAC) is asymptomatic but the homozygous form (HbCC) presents with anemia, tissue anoxia and severe pain.

Beta Thalassemia with variant haemoglobin- This is double heterozygote condition due to coinheritance of β-thalassemia mutation from one parent, and variant β globin chain mutation from other parent. Diagnosed is made by Hb electrophoresis or HPLC.

- One has HbS mutation and other is carrier of β-thalassemia: couple has 25% risk of having child with sickle thalassemia (HbS/β). HbS/β thalassemia produce sickling syndrome of variable severity. Sickling syndromes also occur in individuals who co-inherit HbS with other hemoglobinopathies, such as HbC and HbD.
- HbE/β thalassemia is clinically similar to β-thalassemia intermedia or major.
- HbC/β thalassemia has heterogeneous presentation, from very mild to very severe.

Approach to Prenatal screening for hemoglobinopathy

First prenatal visit
CBC (MCV, MCH)
HPLC (determine Hb type)

Normal CBC and HPLC

HPLC- Hb variant: HbS, E, C, D

No further testing

Testing of partner CBC, HPLC

MCV<80fL, MCH<27pg

elevated HbA2, > 3.5% s/o beta thalassemia trait

Normal HbA2(< 3.5%)

Can be due to Iron deficiency and Alpha thalassemia carrier

Partner HPLC normal

Counsel and reassure

Partner positive for beta thalassemia carrier or Hb variant

Counsel and offer prenatal diagnosis
Indications for prenatal testing and molecular (DNA) diagnosis

<table>
<thead>
<tr>
<th>Both partners beta-thalassemia carriers</th>
<th>DNA analysis of beta globin gene to look for mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>One partner is beta-thalassemia carrier and other is carrier of Hb variant (e.g., HbS, HbE)</td>
<td>DNA analysis of beta globin gene to look for mutation</td>
</tr>
<tr>
<td>Both partners are carriers of HbS</td>
<td>DNA analysis of alpha globin gene to look for gene deletion</td>
</tr>
<tr>
<td>One partner is carrier of HbS and other is carrier of HbC or HbD</td>
<td>DNA analysis of alpha globin gene to look for gene deletion</td>
</tr>
<tr>
<td>One partner is beta-thalassemia carrier and other is alpha-thalassemia carrier.</td>
<td>DNA analysis of alpha globin gene to look for gene deletion</td>
</tr>
<tr>
<td>Both partners are alpha-thalassemia carriers</td>
<td>DNA analysis of alpha globin gene to look for gene deletion</td>
</tr>
</tbody>
</table>

Conclusion
Thalassemia minor is an asymptomatic carrier state that does not limit survival and may never come to medical attention, however if it is present in both the partners then there is 25% risk of having baby with thalassemia major and thus require prenatal counselling and testing. Child with beta thalassemia major will require lifelong regular blood transfusions and majority of complications occur due to iron overload. Severe alpha thalassemia with no production of alpha globin chains (--/--) causes intrauterine death due to hydrops fetalis. Individuals with haemoglobin H (HbH) disease exhibit variable clinical severity, most often a thalassemia intermedia phenotype. Alpha thalassemia trait are generally not symptomatic.

References
INTRODUCTION

Antenatal screening for aneuploidies and neural tube defects has come a long way through the past few decades. The advances in fetal medicine practices has made it possible to identify majority of fetal structural and chromosomal abnormalities by the end of first trimester itself.

Fetal aneuploidy and neural tube defects are major causes of perinatal morbidity and mortality as well as longterm disabilities. All diagnostic prenatal tests used to diagnose fetal aneuploidy carry a risk of miscarriage and are expensive. Therefore, a screening test that has the highest possible detection rate and lowest false-positive rate is of critical importance.

Definition of screening:

It is presumptive identification of unrecognized disease or defect in normal population. In simpler words screen out the high risk from the general population.

Goal is to allocate risk- low risk (screen negative) and high risk (screen positive).

Benefit of screening is that it helps to provide reassurance in case of low risk result while in case of high risk result, we can offer the couple further diagnostic test, which is costlier and also invasive and time consuming.

HISTORY OF ANEUPLOIDY SCREENING

The first method of screening for trisomy 21, introduced in the early 1970s, was based on the association with advanced maternal age. It was apparent that amniocentesis carried a risk of miscarriage and this in conjunction with the financial cost implications, meant that prenatal diagnosis could not be offered to the entire pregnant population.

In the late 1980s, a new method of screening was introduced that takes into account not only maternal age but also the concentration of various fetoplacental products in the maternal circulation.

In the 1990s, screening by a combination of maternal age and fetal NT thickness at 11–13+6 weeks of gestation was introduced.
Subsequently, maternal age was combined with fetal NT and maternal serum biochemistry (free b-hCG and PAPP-A) in the first-trimester to identify about 85–90% of affected fetuses.

In 2001, it was found that in 60–70% of fetuses with trisomy 21 the nasal bone is not visible by ultrasound at 11–13+6 weeks and preliminary results suggest that this finding can increase the detection rate of the first trimester scan and serum biochemistry to more than 95%.

**PRENATAL SCREENING FOR ANEUPLOIDY**

Aneuploidies are chromosomal abnormalities with profound implications on the quality of life of individuals as well as parents. The most common aneuploidy found in live born infants is Trisomy 21 (Downs syndrome), followed by trisomy 18 (Edward syndrome) and Trisomy 13 (Patau syndrome).

The only definite way of diagnosing a chromosomal abnormality in the fetus is by karyotyping the fetal cells obtained by direct testing – chorion villous sampling, amniocentesis, or fetal blood sampling- which is costly, labour intensive and invasive (small risk of pregnancy loss and infection). Therefore it is impractical to apply direct diagnostic testing to all pregnancies.

**CONCEPT OF INVERTED PYRAMID OF ANTENATAL CARE**

First-trimester screening and diagnosis of fetal anomalies is the new Essential in today’s times. Early diagnosis helps in safe and timely termination of affected pregnancy and also provides time to the parents to understand the condition. Every patient should be offered first trimester screening. Rather than concentrating in the third trimester there should be detailed assessment of fetus in the 1st trimester itself.
### Methods Of Screening

<table>
<thead>
<tr>
<th>Methods Of Screening</th>
<th>Components Of The Test</th>
<th>When To Perform Weeks Of Pregnancy</th>
<th>Detection Rate</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (MA)</td>
<td>Age &gt;35 yrs</td>
<td></td>
<td>30%</td>
<td>Obsolete Not recommended</td>
</tr>
<tr>
<td>NT (Nuchal translucency scan)</td>
<td>MA and fetal nuchal translucency (NT)</td>
<td>11–13+6 wks</td>
<td>70–80%</td>
<td>Expertise in USG required</td>
</tr>
<tr>
<td>Combined screening test</td>
<td>MA and fetal NT and maternal serum free b-hCG and PAPP-A</td>
<td>11–13+6 wks</td>
<td>85–90%</td>
<td></td>
</tr>
<tr>
<td>Combined screening test with 1st trimester soft markers</td>
<td>MA and fetal NT and NB and maternal serum free b-hCG and PAPP-A</td>
<td>11–13+6 wks</td>
<td>95%</td>
<td>Recommended method due to high DR and Low false positive rate But requires expertise for USG</td>
</tr>
<tr>
<td>Quadruple Marker test</td>
<td>Maternal serum AFP, uE3, hCG and inhibin-A</td>
<td>16-22 weeks BPD- 32-52 mm</td>
<td>80%</td>
<td>Standard of care in case of missed combined test</td>
</tr>
<tr>
<td>NIPT (Non invasive prenatal test)</td>
<td>Cell free fetal DNA</td>
<td>&gt;10 weeks</td>
<td>&gt;99%</td>
<td>&lt;1% false positive rate Expensive</td>
</tr>
</tbody>
</table>

### Sequential screening (Snijders and Nicolaides 1996)
- Every woman has a risk that her fetus/baby has a chromosomal defect.
- The background or a priori risk depends on maternal age and gestation.
- The individual patient-specific risk is calculated by multiplying the *a priori* risk with a series of likelihood ratios, which depend on the results of a series of screening tests carried out during the course of the pregnancy.
- Every time a test is carried out the a priori risk is multiplied by the likelihood ratio of the test to calculate a new risk, which then becomes the a priori risk for the next test.

### First trimester and second trimester screening

![First trimester and second trimester screening diagram](image-url)
NIPT – Cell free fetal DNA can be done 10 weeks onwards

An ideal Nuchal translucency scan should consist of – Crown rump length, NT, Nasal bone, FHR, comment on Tricuspid regurgitation, Ductus venosus PI, Uterine artery PI and early morphology scan to look for structural anomalies. This scan should be combined with Blood test called Double marker test –

maternal serum free beta-hCG and PAPP-A.
In case if first trimester screening is missed then a genetic sonogram and a quadruple marker test should be performed.

A genetic sonogram consists of detailed sonography of fetus to look for soft markers of trisomy 21. These are not structural abnormalities but just markers of downs syndrome with different likelihood ratios.

These are lateral cerebral ventriculomegaly (mild), absent or hypoplastic nasal bone, increased nuchal fold thickness, intracardiac hyperechogenic focus, aberrant right subclavian artery (ARSA), hyperechogenic bowel, mild hydronephrosis and shortening of the femur or humerus.

**Likelihood ratios of each soft marker**

<table>
<thead>
<tr>
<th>Marker</th>
<th>DR (95% CI) (%)</th>
<th>FPR (95% CI) (%)</th>
<th>LR+ (95% CI)</th>
<th>LR− (95% CI)</th>
<th>LR isolated marker*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracardiac echogenic focus</td>
<td>24.4 (20.9–28.2)</td>
<td>3.9 (3.4–4.5)</td>
<td>5.83 (5.02–6.77)</td>
<td>0.80 (0.75–0.86)</td>
<td>0.95</td>
</tr>
<tr>
<td>Ventriculomegaly</td>
<td>7.5 (4.2–12.9)</td>
<td>0.2 (0.1–0.4)</td>
<td>27.52 (13.61–55.68)</td>
<td>0.94 (0.91–0.98)</td>
<td>3.81</td>
</tr>
<tr>
<td>Increased nuchal fold</td>
<td>26.0 (20.3–32.9)</td>
<td>1.0 (0.5–1.9)</td>
<td>23.30 (14.35–37.83)</td>
<td>0.80 (0.74–0.85)</td>
<td>3.79</td>
</tr>
<tr>
<td>Echogenic bowel</td>
<td>16.7 (13.4–20.7)</td>
<td>1.1 (0.8–1.5)</td>
<td>11.44 (9.05–14.47)</td>
<td>0.90 (0.86–0.94)</td>
<td>1.65</td>
</tr>
<tr>
<td>Mild hydronephrosis</td>
<td>13.9 (11.2–17.2)</td>
<td>1.7 (1.4–2.0)</td>
<td>7.63 (6.11–9.51)</td>
<td>0.92 (0.89–0.96)</td>
<td>1.08</td>
</tr>
<tr>
<td>Short humerus</td>
<td>30.3 (17.1–47.9)</td>
<td>4.6 (2.8–7.4)</td>
<td>4.81 (3.49–6.62)</td>
<td>0.74 (0.63–0.88)</td>
<td>0.78</td>
</tr>
<tr>
<td>Short femur</td>
<td>27.7 (19.3–38.1)</td>
<td>6.4 (4.7–8.8)</td>
<td>3.72 (2.79–4.97)</td>
<td>0.80 (0.73–0.88)</td>
<td>0.61</td>
</tr>
<tr>
<td>ARSA</td>
<td>30.7 (17.8–47.4)</td>
<td>1.5 (1.0–2.1)</td>
<td>21.48 (11.48–40.19)</td>
<td>0.71 (0.57–0.88)</td>
<td>3.94</td>
</tr>
<tr>
<td>Absent or hypoplastic NB</td>
<td>59.8 (48.9–69.9)</td>
<td>2.8 (1.9–4.0)</td>
<td>23.27 (14.23–38.06)</td>
<td>0.46 (0.36–0.58)</td>
<td>6.58</td>
</tr>
</tbody>
</table>

*Derived by multiplying the positive LR for the given marker by the negative LR of each of all other markers, except for short humerus. ARSA, aberrant right subclavian artery; NB, nasal bone.

**WHAT IS LIKELIHOOD RATIO?**

- Likelihood ratio is a number given to each marker
- It tells the probability/chance of a women having a Downs baby because she has tested positive for a marker
- Eg. – if the LR for marker ‘X’ is 5 any woman who tested positive for this marker has a 5 times higher chance of having a Down’s baby
SOFT MARKERS:

• Hypoplastic / absent nasal bone
• Ventriculomegaly

• Thickened nuchal fold
• Short femur/humerus

• Echogenic intra-cardiac focus
• ARSA (aberrant right subclavian artery)

• Echogenic bowel
• Mild pylectasis
COUNSELING

Pretest and post test counseling is a must and should be non directive i.e. The patient should be given the knowledge of all further options available to them and they should be allowed to choose further options accordingly. After counseling the couple may decide to opt or not opt for further tests.

PRENATAL SCREENING FOR NEURAL TUBE DEFECTS

Neural tube defects (NTDs) are among the most common birth defects reported worldwide. The worldwide prevalence of NTDs ranges from 4 to 15 per 10,000 live-births. Extreme forms of NTD such as anencephaly are incompatible with life. In such situations, the pregnancy can be terminated. In other open neural tube defects like - Myelomeningocele - A vaginal route of delivery may have to be avoided as it can add to the neurological deficit in a baby with a spinal meningomyelocele. Post natal surgery and rehabilitation have to be planned. Some patients may have a higher risk of having a baby with NTDs. Timely detection of an NTD helps the family and clinician to cope with the problem more effectively.
Procedures for prenatal diagnosis include: (i) assessment of serum markers such as maternal serum alpha-foetoprotein (AFP) and acetylcholinesterase activity; (ii) prenatal ultrasonography; and (iii) amniocentesis in selected cases. The levels of these two serum markers are increased in neural tube defects and a value of more than two multiples of the median is considered significant. The optimal time for serum screening is 10-20 weeks. In the case of serum markers it is important to apply normative data standardized for a laboratory and the duration of gestation.

Antenatal ultrasonography is a simple, non-invasive and widely available test which has a similar sensitivity with lower false positivity compared to serum markers. Early diagnosis by ultrasound at the time of NT scan is possible but it demands skill and experience in the procedure.

Levels of amniotic fluid alpha-fetoprotein and acetylcholinesterase activity are elevated in neural tube defects. However, increased iatrogenic foetal loss is a disadvantage of this technique.

Detailed counselling of the couple needs to be an integral part of the prenatal screening.

ETHICAL SCENARIO:
All patients should be offered antenatal screening for aneuploidies and NTDs. It may lead to higher number of invasive procedures and sometimes undue anxiety in patients but the final impact of reduction in affected babies will be worth the effort.

CONCLUSION:
Screening for fetal aneuploidies and neural tube defects is the new essential of modern day obstetric care. Education and counseling regarding why to do the test and what to expect – Pre test counseling and explanation of the result – Post test counseling is a must. Counseling should be non directive.

Non invasive prenatal testing is the best available aneuploidy screening method, with highest sensitivity and low false positive rates but highly expensive so not affordable by all couples. The next best screening method is the combined screening which includes a detailed scan and biochemical testing at 11 to 13+6 weeks.

Adopting a protocol for screening and practicing it will make a great difference in present day obstetric care.
This word means a lot of different things for a lot of different people. It's correct Oxford definition, however, is only one.

"The advocacy of women's rights on the grounds of equality of the sexes".

Nothing in those lines suggest violence or misuse of power. So why is that people are so intimidated by a feminist?

Being called a "feminist" has become an insult in today's day and age, the reason for which, I am yet to understand.

I hold resentment towards the phrase,

"Respect her! She's someone's daughter/sister/mother/wife"

Should she not be respected because she is a person? What if she wasn't someone's sister or mother? Would she then deserve disrespect?

FEMINISM

Tanisha Amal
Class -9
St. Joseph convent High School Patna

A real man never hurts a woman.
Be very careful when you make a woman cry. Because God counts her tears The Woman came out of a man's rib, NOT from his feet to be walked on, and NOT from his head to be superior, but from his side to be equal. Under the arm to be protected, And next to the HEART to be loved"
We need to stop respecting women because of their associations with men. Women are people. They have the same feelings and rights as men do.

Perhaps, this is so difficult to understand for us, because we have been brainwashed since an early age.

The Bollywood movies we grew up watching and love, have tons of examples of the hidden misogyny of our society in them. When did it become acceptable to follow a woman around, continuously harass her and touch her without her consent, when she has already said no?

The answer is NEVER!

However, in our Bollywood movies, it is shown that it is okay to publicly harass a woman because-

"Everything is fair in love and war"

How could any of us, Indians, forget the phrase,

" A woman's no is actually a yes".

That is not correct. If she says no, she means no.

**NO MEANS NO .**

The fairy tales that the young girls are told should be altered. From an early age, young girls dream that their "Prince Charming" will come to save them or their "Alladin" will show them the world. The young girls should be taught instead, that they can not only save themselves but also lead an adventurous and interesting life by themselves. Having a partner in their lives is a CHOICE not a necessity.

In the present situation in India, victim blaming is practised like eating food. It comes to us as naturally as that.

Have you ever asked yourself why it becomes mandatory for a girl to wear "salwar-suit" as her school uniform while the boys continue to wear western attires?

To not be a distraction for the male students.

Why can not we teach the male students to respect women rather than have the female students cover every single piece of flesh on their bodies?

That's like accusing a murdered victim by saying - "The murderer will commit a murder. It's in his nature. Why was he roaming outside with his whole body? He was practically begging the murderer to stab him!"

Therefore, STOP VICTIM BLAMING. Educate your kids from a young age about what is right and wrong and teach young girls to take care of themselves.