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Haemovigilance - An Effective Tool For Quality Improvement In Transfusion Pracrtice.

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Abstract :
Haemovigilance is an organized system that incorporates monitoring, identification, reporting, investigating and analysis of adverse episode near-misses and reactions pertinent to transfusion and manufacturing blood products. Approximately, 107 million units of blood donations are collected globally every year. Nearly 50% of these blood donations are collected in high-income countries. Blood donation rate in developed countries is 39.2 donations per 1000 population; 12.6 donations in developing and 4.0 donations in underdeveloped countries. Therefore, in this study Patients with blood transfusion were followed over a period of six months to record the occurance of Adverse reactions due to blood transfusion and its prevalence of occurance based on gender.

Key words: Haemovigilance, Blood transfusion, Adverse reactions.

INTRODUCTION OF HAEMOVIGILANCE.

As per International Haemovigilance Network (IHN) and International Society of Blood Transfusion (ISBT), haemovigilance is described as an assembly of surveillance strategies covering the complete transfusion sequence from the collection of blood and its components to the follow up of its recipients, designed to collect and appraise information on unexpected or undesirable reactions resulting from the therapeutic use of blood products, and to avoid their occurrence and recurrence.

"Haemovigilance is an organized system that incorporates monitoring, identification, reporting, investigating and analysis of adverse episode near-misses and reactions pertinent to transfusion and manufacturing blood products" [(1)].

- Approximately, 107 million units of blood donations are collected globally every year. Nearly 50% of these blood donations are collected in high-income countries. Blood donation rate in developed countries is 39.2 donations per 1000 population; 12.6 donations in developing and 4.0 donations in underdeveloped countries.

SCOPE OF HAEMOVIGILANCE, ITS ESSENTIALITY, TERMINOLOGY:

Ideally, the haemovigilance system should cover all measures and techniques throughout the whole transfusion sequence, from blood donation, processing, and transfusion to patients for the monitoring, reporting, and investigation of adverse events and reactions and near misses pertinent to blood transfusion

- It should be well integrated between the blood transfusion service, hospital staff and transfusion laboratories, transfusion committees, regulatory authorities, and national health agencies.
- An adverse event that results in morbidity or mortality of a recipient is called an adverse reaction and when it affects a donor it is called complication.

NATIONAL HAEMOVIGILANCE PROGRAM OF INDIA:

- Indian Pharmacopoeia Commission in collaboration with National Institute of Biologicals, Noida, and Uttar Pradesh has launched an HvPI on 10th December 2012 across the country under its PvPI, under Ministry of Health and Family welfare, Government of India.
- This is an independent program primarily restricted to voluntary reporting of serious adverse reaction in recipients.
- Fundamental aim of this program is to trail adverse reactions and episodes related to blood transfusion and blood product administration and to help determine the tendency, recommend best practices/policies and interventions required to improve patient care and safety [(1).]

Blood transfusion:

- Blood is most commonly donated as whole blood obtained intravenously and mixed with an anticoagulant. This is usually done as a lifesaving manuver to replace blood cells or blood products lost through severe bleeding, during surgery when blood loss occurs or to increase the blood count in an anaemic patient.
- Red blood cells (RBC) contain haemoglobin, and supply the cells of the body with oxygen. White blood cells are not commonly used during transfusion, but are part of the immune system, and fight infections.
- Plasma is the liquid part of the blood, which acts as a buffer, and contains proteins and important substances needed for the body's overall health.
- Platelets are involved in blood clotting, preventing the body from bleeding [(2).]

Goals of blood transfusion therapy:

- Use of donor erythrocytes with an optimal recovery and half-life in the recipient.
- Achievement of appropriate haemoglobin level.
- Avoidance of adverse reactions, including transmission of infectious agents
- Blood can be provided from two sources: autologous blood (using your own blood) or donor blood (using someone else's blood).

- **Using your own blood (autologous blood):**
  - **Pre-operative donation:** Donating own blood before surgery. The blood bank draws blood and stores it until we need it during or after surgery.
  - **Intra-operative autologous transfusion:**Recycling blood during surgery. Blood lost during surgery is filtered, and put back into body during surgery
  - **Post-operative autologous transfusion:** Recycling blood after surgery. Blood lost after surgery is collected, filtered and returned to body.
  - **Hemodilution:** Donating own blood during surgery. Immediately before surgery, some of blood is taken and replaced with IV fluids. After surgery, blood is filtered and returned. This is done only for elective surgeries. This process dilutes own blood so you lose less concentrated blood during surgery.
  - **Apheresis:** Donating own platelets and plasma. Before surgery, platelets and plasma, which help stop bleeding, are withdrawn, filtered, and returned
- **Donor blood (blood from another person):**
  - All donor blood is tested for safety making its risks very small, but no screening program is perfect and risks, such as contraction of the hepatitis virus or other infectious disease still exist.
  - Volunteer blood: Blood collected from the community blood supply (blood banks). This has the advantage of being readily available, and can be life saving when own blood is not available. The disadvantage is that there is a risk of disease transmission, such as hepatitis, and allergic reactions.
  - Designated donor blood: Blood is collected from the donors selected. Select people with your own blood type who feel are safe donors. Like volunteer blood, there is still a risk of disease transmission, such as hepatitis and AIDS, and allergic reactions.

- **BLOOD BANK:**
  - Blood banks collect, test, and store blood. They carefully screen all donated blood for possible infectious agents, such as viruses, that could make you sick.
  - Blood bank staff also screens each blood donation to find out whether it's type A, B, AB, or O and whether it's Rh-positive or Rh-negative.
  - To prepare blood for a transfusion, some blood banks remove white blood cells. This process is called white cell or leukocyte reduction. Although rare, some people are allergic to white blood cells in donated blood.
  - Not all transfusions use blood donated from a stranger. If going to have surgery, may need a blood transfusion because of blood loss during the operation. If it's surgery that are able to schedule months in advance.
  - If choose to use own blood, will need to have blood drawn one or more times prior to the surgery. A blood bank will store blood for use [(3).]

DOCUMENTING AND REPORTING OF SERIOUS ADVERSE REACTIONS/EVENTS IN BLOOD & BLOOD PRODUCTS TRANSFUSION:

- There are several types of transfusion reactions which can be subdivided in different ways according to the time of occurrence, pathogenesis and / or symptomatology.
- According to the time of occurrence, it is subdivided as:
  a) Acute (< 24 hours after transfusion)
  b) Delayed (> 24 hours after transfusion) reactions.
- As per their pathogenesis, adverse reactions can be further divided as:
  a) Infectious
  b) Non-infectious adverse reactions.
- Major non-infectious acute reactions include:

  1. Acute Hemolytic Transfusion Reactions (AHTR)
  2. Febrile Non-Hemolytic Transfusion Reactions (FNHTR)
  3. Allergic reactions including anaphylactic reactions
  4. Transfusion Associated Acute Lung Injury (TRALI)
  5. Transfusion Associated Circulatory Overload (TACO)
  6. Hypotensive reactions and hyperkalemia.

- Non-infectious delayed transfusion reactions include:

  1. Delayed Hemolytic Transfusion Reactions (DHTR)
  2. Delayed Serological Transfusion Reactions (DSTR)
  3. Post-Transfusion Purpura (PTP)
  4. Transfusion-Associated Graft Versus Host Disease (TAGVHD)
  5. Haemosiderosis.

- The major acute infectious adverse reactions are due to bacterial contamination of the blood component, and delayed infectious reactions may be due to viral (e.g., hepatitis B / C, HIV) or parasitic (e.g., malaria) transmission [(4).]

Adverse reaction

- An adverse event is an undesirable and unintended occurrence before, during or after transfusion of blood or blood component which may be related to the administration of the blood or component

- An adverse reaction is an undesirable response or effect in a patient temporally associated with the administration of blood or blood component.

Table 1. Blood transfusion Adverse reactions and management [5; 4; 6].

Reaction	Signs and Symptoms	Prevention	Management	Frequency
Febrile (non-haemolytic transfusion reaction):	**Mild:** Fever, chills, Rigor. **Moderate:** Fever **Severe:** Fever, chills, Tachycardia, respiratory distress.	Check previous history. Give paracetamol 1g PO.	Check label and recipient identity. Antipyretic paracetamol 1g PO.	1-3:100 (higher in multiple transfusions)
Allergic reaction (Minor):	Flushed skin, urtricaria, edema of lips and tongue.	Prophylaxis with anti-histamine- Cetirizine 10 mg PO.	Slow transfusion, check label and recipient identity, anti-histamine.	1:100-1:500
Allergic reaction (moderate):	Cough, hypotension, Dyspnoea.	Prophylactic Treatment with Anti-histamine or Hydro-Cortisone	Stop transfusion, Check label and recipient identity. IV fluids, Oxygen, anti-Histamine.	1:500- 1:5000
Anaphylactic allergic reaction (severe):	Shock, tachycardia, wheezing, itching, severe, anxiety.	Ig E deficiency or to have anti- Ig A.	Stop transfusion, Adrenaline 1:1000 IM, Hydrocortisone 4mg/kg,Antihistamine – 10mg.	1:20000 - 1:50000.
Hypotensive reaction:	Hypotension (BP less than 30mmHg**)**	----------	Stop transfusion, Replace IV set and infuse saline.	1-2:1000
Transfusion Associated Graft Vs Host disease:	Fever, rashes, Liver dysfunction, Diarrhoea, Pancytopenia.	Cellular blood components to inactivate residual lymphocytes.	Consult Haematologist and investigate diagnosis.	Rare but fatal.
Post transfusion purpura:	Thrombocytopenia often with purpura.	Restrictive transfusion practice.	Consult haematologist. Test for HPA antibody.	Lesser than 1:100000.
Transfusion Associated Circulatory Overload (TACO):	Increased BP, dyspnoea, Pink frothy sputum, Oxygen desaturation.	Transfuse at a rate appropriate for recipient. Avoid transfusion at night.	Stop transfusion & Furosemide 1- 2mg/kg IV.	1:100-1:1000.
Bacterial sepsis:	Rigors, chills, Wheezing, respiratory distress, Explosive diarrhoea	Visibly clumped platelets. Unusual dark red cells punctured or leaking back	Stop transfusion. Broad spectrum antibiotics – Cephalosporin and Gentamycin 5mg/kg.	Platelet <1:10000, Red cell<1:250000

Risks:

1) **Allergic Reactions:**

- Some people have allergic reactions to the blood given during transfusions. This can happen even when the blood given is the right blood type.

2) Allergic reactions can be mild or severe. Symptoms can includes - Anxiety, Chest and/or back pain, Trouble breathing, Fever, chills, flushing, and clammy skin, A quick pulse or low blood pressure, Nausea (feeling sick to the stomach)

3) **Viruses and Infectious Diseases:**

- Some infectious agents, such as HIV, can survive in blood and infect the person receiving the blood transfusion. To keep blood safe, blood banks carefully screen donated blood.
- The risk of catching a virus from a blood transfusion is very low
  - **Hepatitis B and C ,HIV**: 1 in 2 million
  - **Variant Creutzfeldt-Jakob disease (vCJD): very rare**

4) **Iron Overload:**

- Getting many blood transfusions can cause too much iron to build up in your blood (iron overload) (7). People who have a blood disorder like thalassemia, which requires multiple transfusions, are at risk for iron overload.

❖ **Possible Complications of a Transfusion Reaction:**

1. Pulmonary edema – when the lung collects excess fluids
2. Acute kidney failure
3. Anaemia
4. Shock resulting from inadequate blood flow (8).

❖ **Steps for managing suspected transfusion reactions:**

a. Stop the transfusion immediately.
b. Check and monitor vital signs.
c. Maintain intravenous (IV) access (Do not flush existing line and use a new IV line if required).
d. Check the right pack has been given to the right patient.
e. Notify your Medical Officer and Transfusion Service Provider (9).

TREATMENT OF TRANSFUSION REACTIONS:

- Continuous monitoring of vital signs during generalized anaesthesia may prevent acute circulatory (volume) overload, but it may not detect early signs of other reactions (eg, acute haemolytic transfusion reactions).
- The onset of red-coloured urine in a transfused patient should raise the question of a haemolytic transfusion reaction.

Various medications can be given such as:
Antihistamines, Antipyretic, Steroids, Bronchodilators, Vasopressors, IVfluids

In other cases such as

1. **Allergic reactions:** Diphenhydramine is usually effective for relieving pruritus that is associated with hives or a rash
2. **Volume Overload** in Patients with cardiopulmonary disease and infants during rapid transfusion. Stop the transfusion; administer oxygen and diuretics as required.
3. **Hypothermia:** Appropriately maintained blood warmers should be used during massive or exchange transfusion
4. **Citrate toxicity:** Citrate is the anticoagulant used in blood products. It is usually rapidly metabolised by the liver.Slowing or temporarily stopping the transfusion allows citrate to be metabolised.
5. **Potassium Effects:** Stored red cells leak potassium proportionately throughout their storage life. At RCH red cells are irradiated just prior to issue. Blood less than 7 days old is generally used for rapid large volume transfusion in small infants. Irradiation of red cells increases the rate of potassium leakage

6. **Delayed and Long Term Adverse Effects of Transfusion:** Patients may develop antibodies to red cell antigens. Antibodies can occur naturally, or may arise as a consequence of previous transfusion or pregnancy. An antibody screen is performed as part of pre-transfusion testing. When an antibody is detected, it is identified and appropriate antigen negative blood is provided. Sometimes antibodies fall below detectable limits and may not be detected by pre transfusion testing.
7. **Alloimmunisation:**
   a) Red Blood Cells : Patients experiencing alloantibody formation are asymptomatic. Alloimmunisation to the D and K (Kell) antigens is prevented by the provision of Rh (D) negative and Kell negative blood for Rh (D) negative, Kell negative patients. This is important for females with child-bearing potential as these antibodies can cause severe haemolytic disease of the new-born during pregnancy.
   b) Platelets : Immunological causes include the development of antibodies to human leucocyte antigens (HLA) or human platelet antigens (HPA).Immunological refractoriness can be managed by the provision of HLA or HPA matched platelets. Leucocyte reduction of blood products to levels less than 106/unit reduces the likelihood of alloimmunisation
8. **Immunomodulatory effects:** Unknown, possibly mediated by donor white cells or plasma. Not known, possibly leucocyte depletion of blood products [10; 11; 12].

THALASSEMIA

- They are inherited blood disorders characterized by decreased haemoglobin production.
- Symptoms depend on the type and can vary from none to severe
- Often there is mild to severe anaemia (low red blood cells or haemoglobin).
- Anaemia can result in feeling tired and pale skin. There may also be bone problems, an enlarged spleen, yellowish skin, and dark urine. Slow growth may occur in children.
- Thalassemia's are genetic disorders inherited from a person's parents.
- There are two main types, alpha thalassemia and beta thalassemia.
- The severity of alpha and beta thalassemia depends on how many of the four genes for alpha globin or two genes for beta globin are missing.

Alpha-thalassemia:

- The α-thalassemia involves the genes *HBA1*and *HBA2*, inherited in a Mendelian recessive fashion.
- Two gene loci and so four alleles exist. Two genetic loci exist for α globin, thus four alleles are in diploid cells.
- Two alleles are maternal and two alleles are paternal in origin
- Alpha-thalassemia's result in decreased alpha-globin production, therefore fewer alpha-globin chains are produced, resulting in an excess of β chains in adults and excess γ chains in new-borns.

Beta-thalassemia:

- Beta thalassemia's are due to mutations in the *HBB gene* on chromosome 11, also inherited in an autosomal, recessive fashion.
- The severity of the disease depends on the nature of the mutation and on the presence of mutations in one or both alleles.
- Mutated alleles are called β^+ when partial function is conserved (either the protein has a reduced function, or it functions normally but is produced in reduced quantity) or β^o, when no functioning protein is produced.
- β thalassemia major (Mediterranean anaemia or Cooley anaemia) is caused by a β^o/β^o genotype. No functional β chains are produced, and thus no haemoglobin A can be assembled. This is the most severe form of β-thalassemia.
- β thalassemia intermedia is caused by a β^+/β^o or β^+/β^+ genotype. In this form, some haemoglobin A is produced;

- β thalassemia minor is caused by a β/β^{o} or β/β^{+} genotype. Only one of the two β globin alleles contains a mutation, so β chain production is not terribly compromised and patients may be relatively asymptomatic (13; 14).

AIM:

Assessing, monitoring and reporting adverse reactions in Blood transfusion practice for quality improvement in Haemovigilance program.

OBJECTIVES:

- To analysis adverse reactions in blood transfused patients.
- Monitor transfusion reactions.
- Create awareness among health care professionals.
- To promote, enable and maintain a high level of ethical medical and scientific standards in blood transfusion science.
- To contribute the advancement of knowledge in the field of blood transfusion.
- To identify trends, recommend best practices and interventions require to improve patient care and safety of blood, while reducing overall cost of health care system.

MATERIALS AND METHODS:

STUDY DESGIN: A prospective observational study.
STUDY DURATION: The study was conducted in following six months duration i.e.; from September 1st 2022 – February 18th 2023.
STUDY SITE: The study was conducted at District Government hospital, Eluru, West Godavari district.
STUDY POPULATION: Study population size – 1000 patients are taken into study.
STUDY METHOD: Prospective observational study.
SOURCE OF DATA AND MATERIALS:
Patient specific proforma was designed, the patients consent information and data required for the study is gathered from the Blood bank daily and we approached the patients by oral questioning whether any adverse reactions were observed before/during/after the blood transfusion and the data is documented.

STUDY CRITERIA:
INCLUSION CRITERIA:

- Patients who are involved in blood transfusion.
- Patients who are Anaemic.
- Anaemic, Labour, Dialysis, Thalassemia, Ortho patients were involved.
- Post-Operative patients were also involved in the study.

EXCLUSION CRITERIA:

- Trauma patients were excluded.

DATA MANAGEMENT AND STUDY PROCEDURE:

- The obtained patient specific data were entered into data proforma.
- Oral questioning regarding the adverse reactions is observed after transfusion.
- The reaction which was observed was collected, documented in proforma.

STATISTICAL ANALYSIS:

- Graphical representation like bar graph and pie chart were used for visual interpretation to analyse the data.

RESULTS :

Table 2:Distribution of people according to age and gender.

Age in years	Male patients	Female patients
1 – 10	15	3
11 – 20	32	110
21 – 30	30	365
31 – 40	33	83
41 – 50	58	59
51 – 60	69	33
61 – 70	36	32
71 – 80	13	17
81 – 90	7	4
91– 100	1	0
TOTAL	294	706
Grand total	1000	

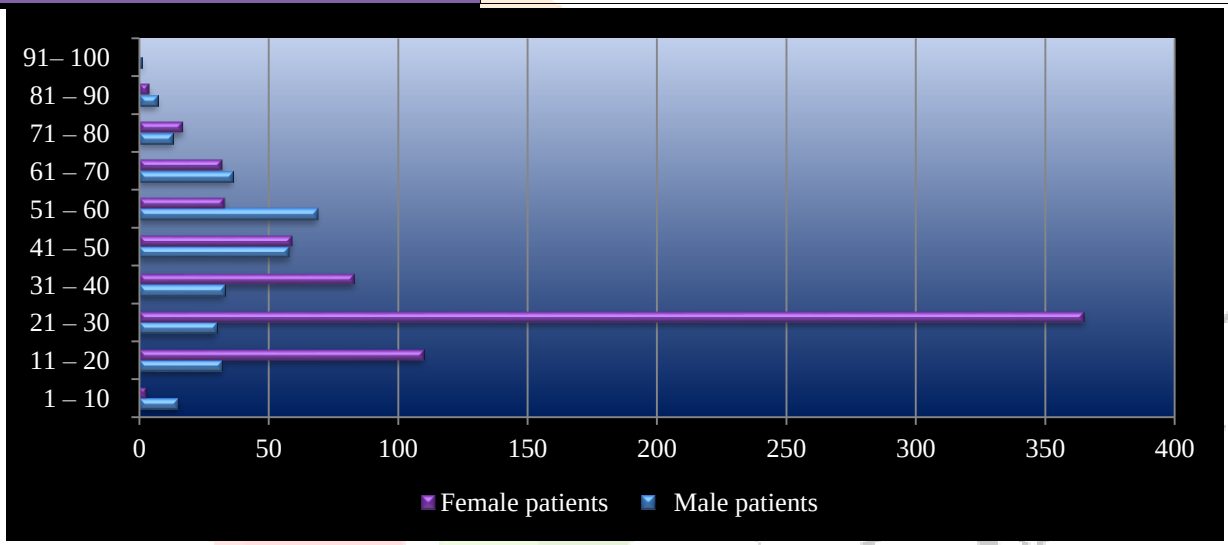

Figure 1: Age and gender wise distribution of people

The above (RESULTS :

Table 2,Figure 1) show the number of people taken in the study with age range and gender. From the above information we found that female patients are more in number and also their proportion is high at the age ranges (11-40 years). Having number of female population at 21-30years of age range i.e. 365(female) and most number of male population at 51-60years of age range i.e. 69(male).

Table 3:Distribution of people according to diagnosis.

DIAGNOSIS	TOTAL	WITH AR	WITHOUT AR
THALESSEMIA	32	32	0
DIALYSIS	73	20	53
LABOUR	206	6	200
ANTENATAL	119	4	115
POST NATAL	64	3	61

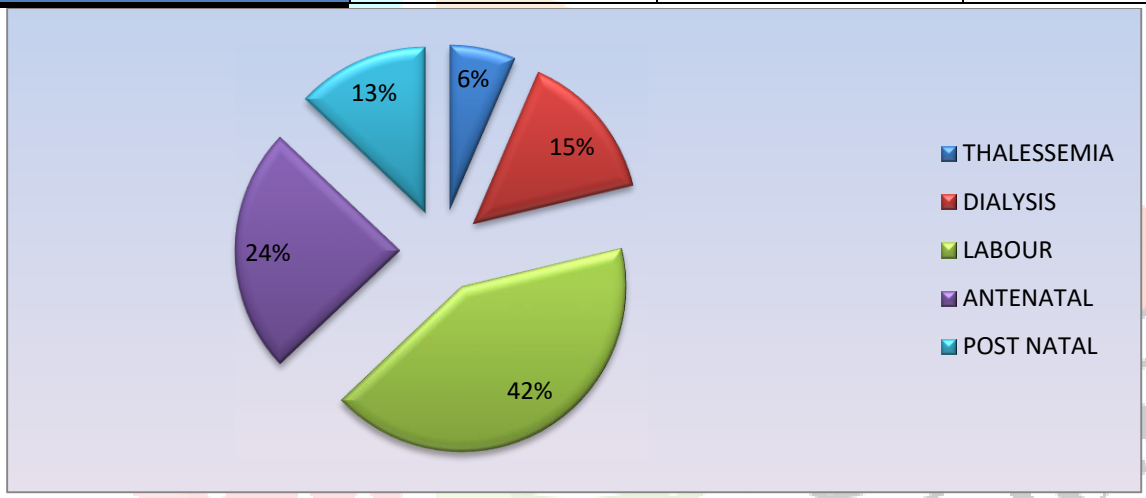

Figure 2: Pie chart of the table above.

The above (Table 3Figure 2) show the people distributed according to the diagnosis.

Table 4: Distribution of patients having Adverse effects based on gender.

	Male		Female		Total with AR
	With AR	without AR	With AR	without AR	
No.of patients	41	291	37	631	78
percentage(%)	14.1		5.9		20.0

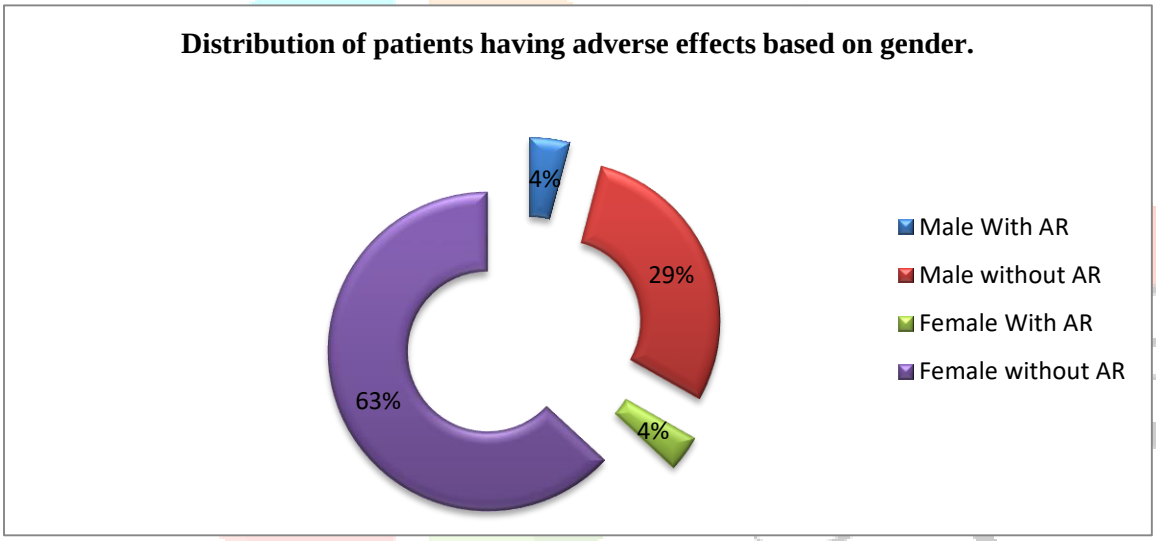

Figure 3: Distribution of patients having adverse effects based on gender.

Table 3 and figure 3 show the distribution of patients having Adverse drug reaction based on gender.

Table 5: Distribution of patients based on their diagnosis and gender.

DIAGNOSIS	Total	With AR	Male	Female
THALESSEMIA	32	32	15	17
DIALYSIS	73	20	9	11
LABOUR	206	6	3	3
ANTENATAL	119	4	2	2
POST NATAL	64	3	1	2
OTHERS/UNDEFINED	506	13	6	7
TOTAL	1000	78	37	41

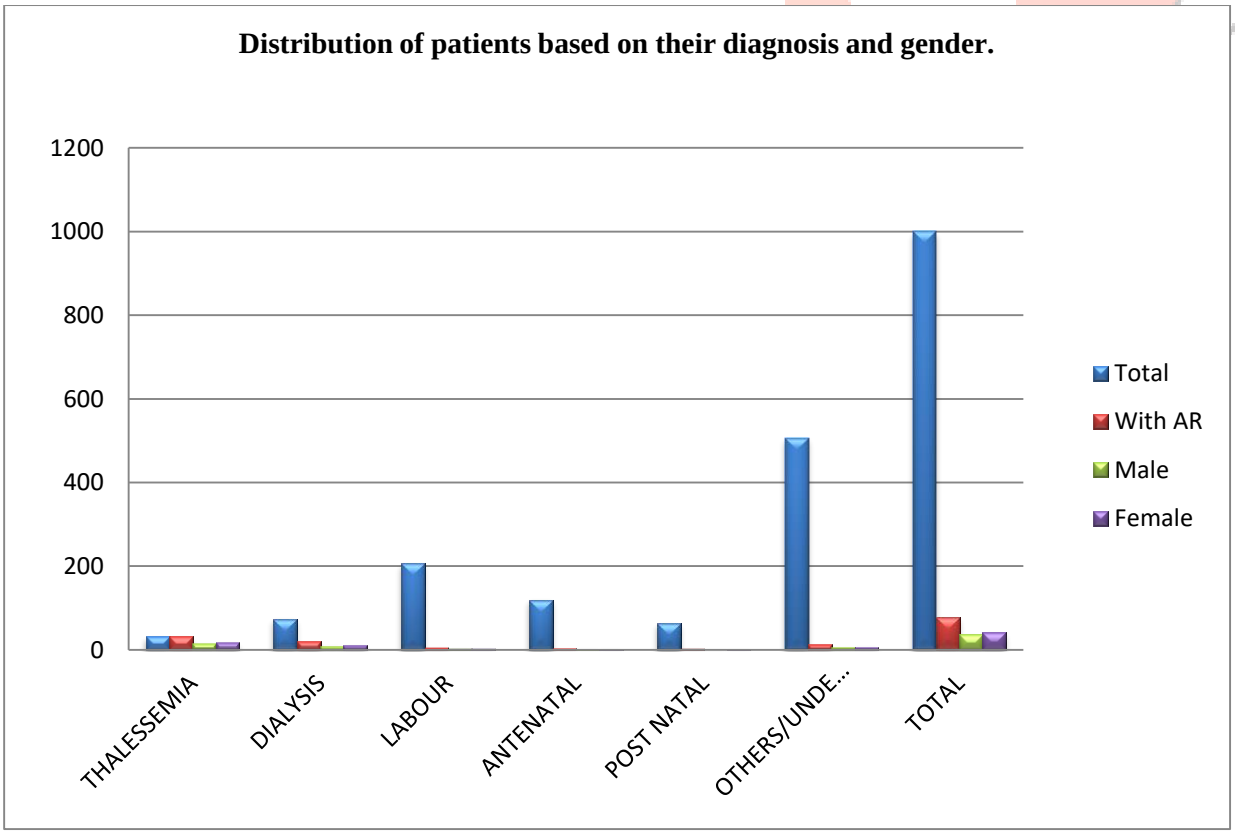

Figure 4: Distribution of patients based on their diagnosis and gender.

Table 4 and figure 4 show the Distribution of patients based on their diagnosis and gender.

Table 6: Distribution of patients having ARs based on their age and gender.

Age in years	Male patients	Male%	Female patients	Female%
1 – 10	13	31.7	3	8.1
11 – 20	7	17.1	11	29.7
21 – 30	3	7.3	14	37.8
31 – 40	1	2.4	2	5.4
41 – 50	3	7.3	5	13.5
51 – 60	10	24.4	1	2.7
61 – 70	3	7.3	1	2.7
71 – 80	0	0.0	0	0.0
81 – 90	0	0.0	0	0.0
91– 100	1	2.4	0	0.0
TOTAL	**41**	**100.00**	**37**	**100.00**
Grand total	**1000**			

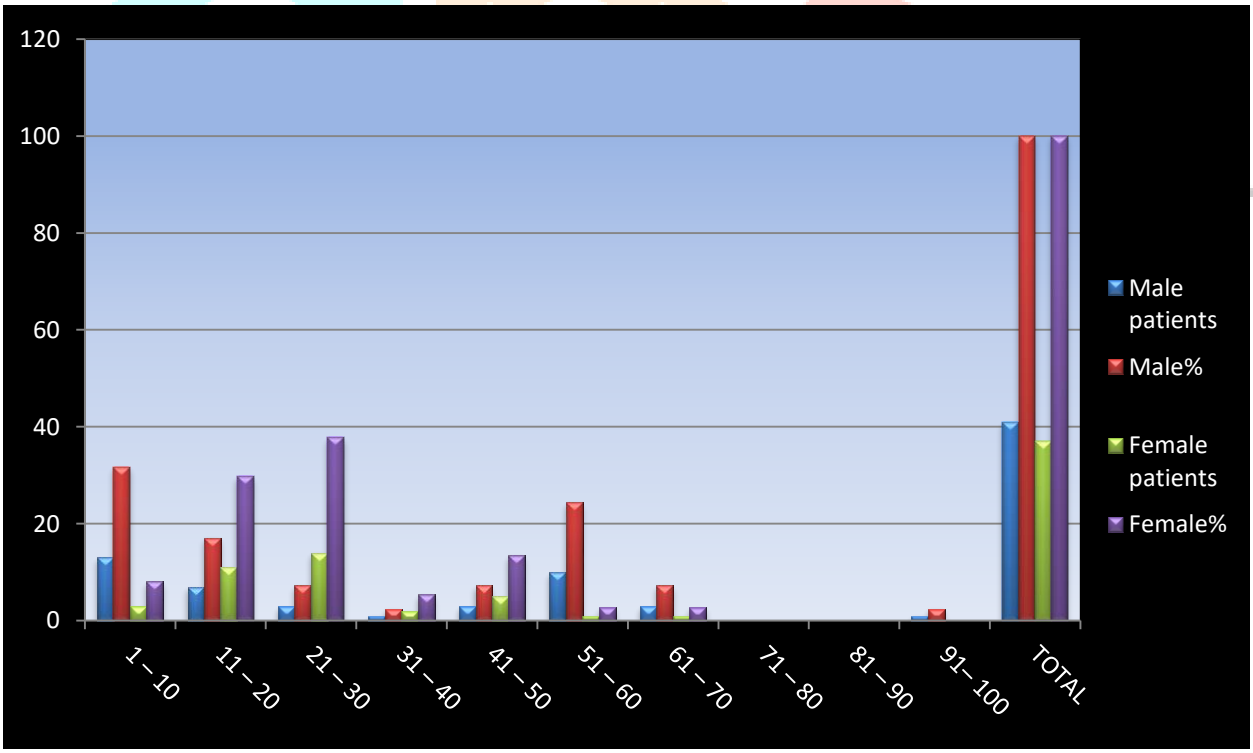

Figure 5: Distribution of patients having ARs based on age and gender.

DIFFERENTIATION BETWEEN MALE AND FEMALE PATIENTS IN BLOOD TRANSFUSION PRACTICE

As compared with both male and female patients by monitoring adverse reactions among them, the final outcome shows “Male and female patients were equally effected with adverse reactions”.

Test of hypothesis: To observe whether any difference between male and female patients**.**

Null hypothesis: Both male and female patients are equally effected with adverse reactions.

Alternative hypothesis: Both male and female patients are not equally effected with adverse reactions.

Table 7: t-Test: Paired Two Sample for Means.

t-Test: Paired Two Sample for Means.		
	Male	*Female*
Mean	0.1025	0.09984
Variance	0.0124236	0.0165418
Observations	10	10
Pearson Correlation	0.1793634	
Hypothesized Mean Difference	0	
df	9	
t Stat	0.0544985	
P(T<=t) one-tail	0.4788643	
t Critical one-tail	1.8331129	
P(T<=t) two-tail	0.9577286	
t Critical two-tail	2.2621572	

Comparison: In t-test, calculated value is lesser than table value. Hence we accept null hypothesis and reject alternative hypothesis.

OBSERVATION AND DISCUSSION

The main aim of our study is to assess, monitor and report adverse reactions in blood transfusion practice for quality improvement in Haemovigilance program.

In our present study, a total of 1000 blood transfusion patients were considered. We had divided them into male and female patients of which total male patients are 332 in number and total female patients in our study are 668 in number. From them, we have sub-categorised total patients according to disease wise such as surgical ward, Orthopaedic, Neuro, General ward patients. Apart from them we considered other groups of patients according to higher incidence such as Thalassemia, Dialysis, Antenatal, Postnatal, Labour patients. We have excluded Trauma care unit patients from our study population.

The maximum number of patients who are affected with adverse reactions belongs to the age group for Male are likely to be from 1- 10 years (as most of them were Thalassemia patients – 32.5%) and 51-60 years age group (25%) were mostly affected with adverse reactions. For Female patients are from age group of 21-30 years (36.8%) followed by 11-20 years (28.9%).

We observed in our study, all patients after receiving blood transfusion only they had developed the adverse reactions. None of them were developed reactions before/during blood transfusion. The commonly observed reactions we found in our study are Headache, fever, chills, vomitings, urtricaria, itching, nausea, loss of appetite, body pains, dyspnoea. The main reasons for developing these reactions were found to be:

Conclusion: Both male and female patients are equally affected with adverse reactions.

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