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Side Effects Associated With Chemotherapy of Acute Lymphocytic Leukemia with Vincristine and Anthracyclines

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ABSTRACT

Background: Acute lymphocytic leukemia or acute lymphoblastic leukemia is a malignant (clonal) disease of the bone marrow in which early lymphoid precursors proliferate and replace the normal hematopoietic cells of the marrow. It is characterized by the overproduction of immature white blood cells, called lymphoblast or leukemic blasts. Chemotherapy of cancer has many side effects. Use of vincristine and anthracyclines can lead to many side effects. It may limit the efficacy of work in daily life activities of the patient. **Aim:** The aim of this study is to evaluate the side effects associated with the use of vincristine and anthracyclines. **Methodology:** This study was conducted with the objective to assess and evaluate the side effects of vincristine and anthracyclines in MNJ Institute of Oncology and Regional Cancer Centre (RCC), Lakdikapul, Hyderabad. This study is observational in nature and the subjects enrolled under this study were about 64. Informed consent was obtained from all the subjects. Subjects recruited in this study were admitted as in patients in the hospital to receive chemotherapy. The assessment of quality of life is done by using EORTC QLQ- C30 questionnaire. **Results:** In this study, a total of 64 subjects with cancer were evaluated. Of 64 patients included, about 51.565 belong to age group of 0-14 years, followed by 18% in age group 15-24 years. Indicating the higher incidence of ALL in children's specifically and the family history of non- specific cancer was found in 3 patients in the study. During the study most common side effects observed were nausea (24), vomiting (22), and shortness of breath (37) and chest pain (30) which ranges from mild to moderate in severity. **Conclusion:** Among 64 subjects undergoing CT for ALL, out of them ALL was dominantly diagnosed in males (89%). Of 64 patients studied, 57 patients experienced leukocytopenia, 38 experienced neutropenia, 46 experienced thrombocytopenia and anemia in 44 patients. Thus, increased rate of transfusions (45 in males, 5 in females) attributed to decreased quality of life of patients. 1 male and 1 female died during the study, due to SOB due to bilirubinemia and non-adherence to the CT.

Key words:

Cancer,
Acute lymphocytic leukemia,
Vincristine, Anthracyclines.

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INTRODUCTION

Human body is made up of trillions of cells. Cancer can start anywhere in these cells. These cells start to divide uncontrollably and even spread to other cells. Sometimes these affected cells can move to far places through blood or lymph and form new tumor¹. The two types of cancers are benign tumors and malignant tumors. The Benign tumors are located at a particular place in the body. They do not have the ability to spread to other parts of body. Uncontrollable growth is not seen in this tumor. In Malignant tumors, the infected cells enter and destroy the organs and healthy tissues present around it. They may or may not be cancerous². In India, one woman dies of cervical cancer every 8 minutes. For every 2 women newly diagnosed with breast cancer, one woman dies of it in India. As many as 3500 persons die every day due to tobacco-related diseases in India. Estimated number of people living with the disease is around 2.25 million. Every year over 11 lakhs new cancer patients are registered. Cancer of oral cavity and lungs account for 25% of cancer deaths in males and cancer of breast and oral cavity accounts for 25% cancers in females³.

Mostly cancer is caused due to mutations in the DNA present in the cells. (4)Other causes of cancers include, Physical activity, Diet, Exposure to harmful rays due to radiation or sun, Idiopathic causes.(2) Depending on the part of the body affected,

the signs and symptoms of cancer vary.(4) Mostly they appear in the form of weight loss or tiredness for more than few weeks.(2) General signs and symptoms include: Fatigue, Appearance of a lump that can be felt, Unexplained weight loss or weight gain, Bowel or bladder habit changes, Difficulty in swallowing, Sudden onset of fever or night sweats, Trouble in breathing, Hoarseness, Changes in appearance of skin such as darkening, yellowing or redness of skin, Discomfort after eating or indigestion⁴. Different types of cancers have different type of treatments. Various types of treatments include: Surgery, Radiation therapy, Chemo therapy, Hormone therapy, targeted therapy and Immunotherapy^{5,6}.

Leukemia Begins in a cell in the Bone marrow. Then the cell undergoes a change and becomes a type of leukemia cell. After leukemic change, the leukemia cells may grow and survive better than normal cells. Over time, the leukemia cells suppress the development of normal cells. After diagnosis and treatment, many people with leukemia live many good, quality years. The different types of leukemia includes: Acute lymphoblastic leukemia (ALL), Acute myeloid leukemia (AML), Chronic lymphocytic leukemia (CLL), Chronic myeloid leukemia (CML), Biphenotypic acute leukemia (BAL). The other types of leukemia that are uncommonly seen are: Hairy cell leukemia, T cell prolymphocytic leukemia and Juvenile myelomonocytic

leukemia⁷. Acute lymphocytic leukemia or acute lymphoblastic leukemia is a malignant (clonal) disease of the bone marrow in which early lymphoid precursors proliferate and replace the normal hematopoietic cells of the marrow. It is characterized by the overproduction of immature white blood cells, called lymphoblasts or leukemic blasts. These cells crowd the bone marrow, preventing it from making normal blood cells. The exact cause of ALL remain unknown but it is thought to result from mutations in one or more of the genes that normally control blood cell development. But, certain factors have been identified that may increase the risk of ALL. It includes: Previous cancer treatment, Exposure to radiation, Genetic disorders, Having a brother or sister with ALL. Signs and symptoms of ALL include: Bleeding from the gums, Bone pain, Fever, Frequent infections, Lumps caused by swollen lymph nodes in and around the neck, underarm, abdomen or groin. Shortness of breath, Blood clots, Palpable lymphadenopathy⁸. Vincristine is an anti- cancer chemotherapy drug. It is classified as a plant alkaloid. It can be used in the treatment of Acute leukemia, Hodgkin's and Non- Hodgkin's lymphoma, Neuroblastoma, Rhabdomyosarcoma, Ewing's sarcoma, Wilms tumor, Multiple myeloma, Chronic leukemia's, Thyroid cancer, Brain tumors. It can also be used in some types of blood cancers. Vincristine is given as intravenous infusion or intravenous injection⁹. Anthracyclines are anti- cancer compounds, obtained from Streptomyces bacteria. It includes: Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Valrubicin¹⁰.

MATERIALS AND METHODS

METHODOLOGY

STUDY SITE

The study was carried out at MNJ Institute of Oncology and Regional Cancer Centre (RCC)

STUDY DESIGN

Prospective and Retrospective study.

STUDY PERIOD

The study was conducted for 6 months (September 2018 to February 2019).

SAMPLE SIZE

Patients recruited in the study with cancer were inpatients from the hospital. A total of 64 patients including 57 males and 07 females were taken and that who fulfilled the inclusion criteria.

STUDY CRITERIA

Inclusion Criteria

- Patients undergoing chemotherapy of ALL with vincristine and Anthracyclines.
- Patients who are conscious and cooperative.
- Patients who are willing to participate in the study.
- Patients of age group between 5-60 yrs.

Exclusion Criteria

- Patients with serious psychiatric illness or underwent recent surgery.
- Patients who are not conscious and communicate verbally.

- Non-compliant patients.
- Patients with co-morbid conditions.

A suitable data collection form was designed to collect, document, and analyze the data. Data collection form that includes provision to collect information like demographic details (name, age, sex), past medical history, family history, diagnostic parameters, prescribed drugs, chemotherapy induced side effects, re-visit details and contact details.

RESULTS AND DISCUSSION

1. DISTRIBUTION BASED ON GENDER

In this study, a total of 64 patients who were diagnosed with Acute lymphocytic leukemia (ALL), among whom the majority were males, who constituted account of 89%(n= 57) and females constituted 11%(n= 07).

Tab1: Distribution based on Gender

GENDER	NO. OF PATIENTS	PERCENTAGE (%)
MALE	57	89
FEMALE	7	11
TOTAL	64	100

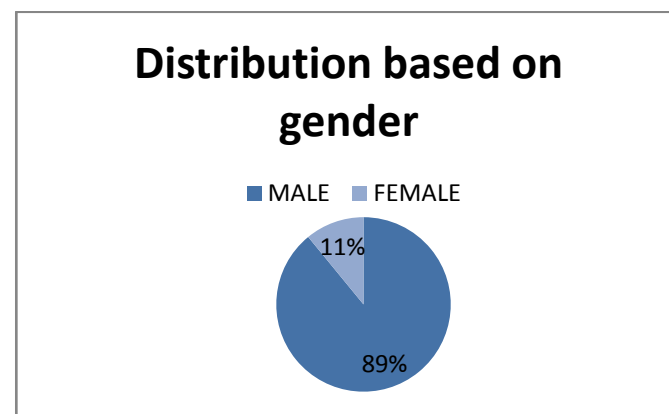


Fig 1: Distribution based on Gender

2. DISTRIBUTION BASED ON AGE OF THE PATIENT

According to the age group analysis, no. of cases in age group of children's (0-14) were 51.56% (n= 33), Teenagers and Young adults age group (15-24) were 28.12% (n= 18), Adulthood age group (25-49) were 18.75% (n=12), Late adulthood age group (50-74) were 1.44% (n= 01), and elderly age group (>75) were 0 (n= 0).

Tab2: Distribution based on age of the patient

AGE GROUP	NO. OF PATIENTS	PERCENTAGE (%)
Children (0-14)	33	51.56
Teenagers & Young Adults (15-24)	18	28.125
Adulthood (25-49)	12	18.75
Late Adulthood (50-74)	1	1.44
Elderly (>75)	0	0
Total	64	100

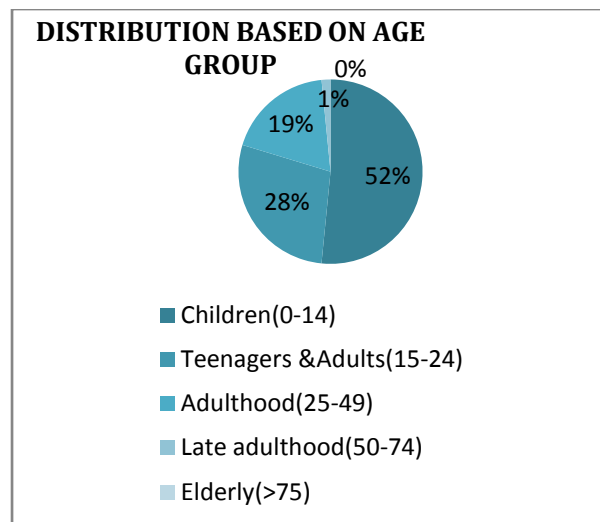


Fig 2: Distribution based on age of the patient

3. DISTRIBUTION BASED ON BLOOD PARAMETERS

According to the Blood parameters analysis, Leukocytopenia was seen in 89% (n= 57) of the patients, Neutropenia was seen in 59.3% (n= 38) of the patients, Thrombocytopenia was seen in 71.8% (n= 46) of the patients and Anemia was seen in 68.7% (n= 44) of the patients.

Tab3: Distribution based on blood parameters.

BLOOD PARAMETER	FREQUENCY	PERCENTAGE (%)
Leukocytopenia	57	89
Neutropenia	38	59.3
Thrombocytopenia	46	71.8
Anemia	63	98.7

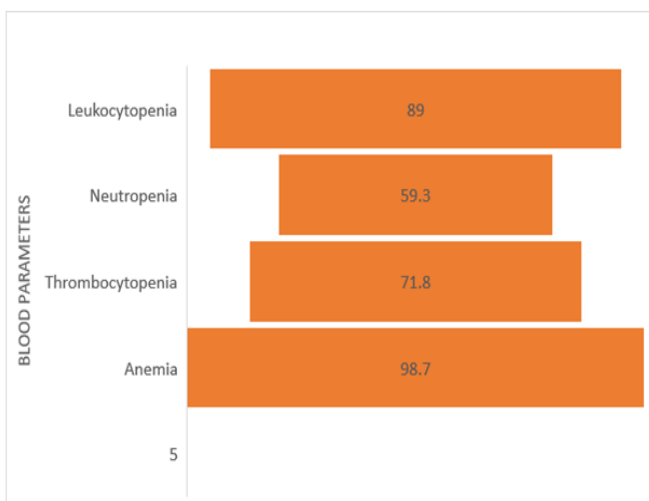


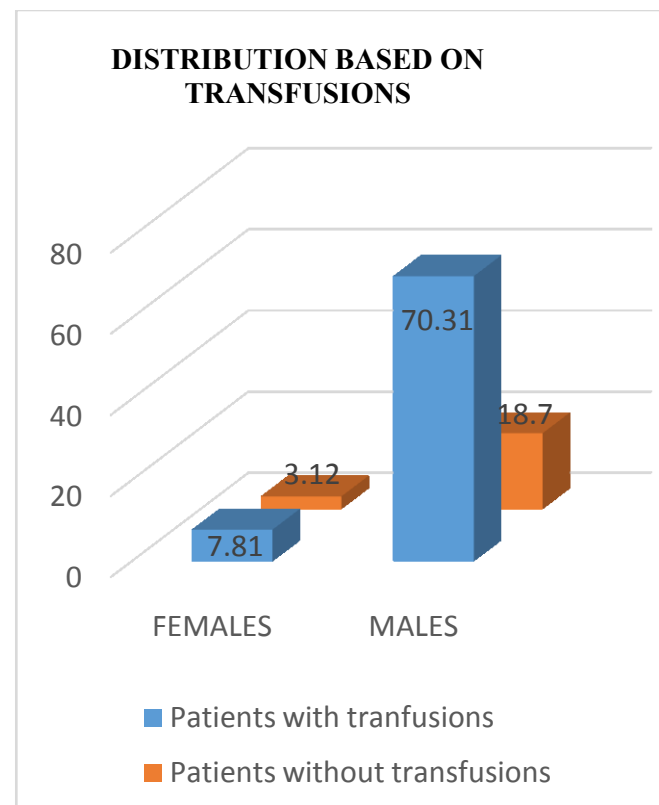
Fig 3: Distribution based on blood parameters

4. DISTRIBUTION BASED ON NUMBER OF TRANSFUSIONS:

In this study, a total of 64 patients who were diagnosed with Acute lymphocytic leukemia (ALL), among whom Females 7.81% (n= 5) and Males 70.31% (n= 45) had taken transfusions. Females 3.12% (n= 2) and Males 18.75% (n= 12) had not taken transfusions.

Tab4: Distribution based on number of transfusions

GENDER	WITH TRANSFUSIONS (%)	WITHOUT TRANSFUSIONS (%)
FEMALES	5 (7.81)	2 (3.125)
MALES	45 (70.31)	12 (18.75)



5. VINCRISTINE AND ANTHRACYCLINES DOSE AND ROA:

Table 5: Vincristine and Anthracyclines dose and ROA.

Drug	Dose	Route of administration(ROA)
VCR	1 – 1.5 mg	iv infusion / push
Doxorubicin	10- 40 mg	iv/ im

Other drugs commonly administered during chemotherapy of ALL

Drugs	Dose/Route of administration
Leunase (L-asparaginase)	1000 units/im
Wysolone (prednisolone)	20mg/PO
Rantac (ranitidine)	150mg/Po
Zofer (ondansetron)	8mg/iv/PO
Endoxan (cyclophosphamide)	1g/iv
MTX (methotrexate)	2.5mg/PO
6-MP (6 mercaptopurine)	50mg/PO
Dexa (dexamethasone)	8mg/iv push
Tramadol	50mg/PO
Zyloric (allopurinol)	100mg/PO
Syscan (fluconazole)	200mg/PO

Table 6: Other drugs commonly administered during chemotherapy of ALL**6. SIDE EFFECTS****Tab 7: Side effects**

SIDE EFFECTS	NOT AT ALL		MILD		MODERATE		SEVERE	
GENDER(M/F)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)
NAUSEA	14.8	14.3	35.2	42.9	40.7	28.6	9.3	14.3
VOMITING	13	42.9	16.7	0	38.9	42.9	31.5	14.3
DIARRHEA	35.2	57.1	18.5	0	38.9	42.9	7.4	0
MOUTHSORES	27.8	57.1	25.9	0	18.5	42.9	27.8	0
SHORTNESS OF BREATH	14.8	0	20.4	57.1	37	14.3	27.8	28.6
CHEST PAIN	27.8	0	53.7	71.4	9.3	14.3	9.3	14.3
ALOPECIA	35.2	28.6	27.8	42.9	16.7	14.3	20.4	14.3
TINGLING OF LIMBS	42.6	0	24.1	14.3	24.1	71.4	9.3	14.3
PAIN DURING MICTURATION	64.8	42.9	29.6	57.1	5.6	0	0	0
HEADACHE	68.5	57.1	24.1	42.9	5.6	0	1.9	0
VISION/HEARING DISTURBANCE	83.3	57.1	11.1	42.9	5.6	0	0	0
LOSS OF WEIGHT	55.6	42.9	37	57.1	5.6	0	1.9	0
PAIN	20.4	42.9	24.1	14.3	29.6	42.9	25.9	14.3

FREQUENCIES OF SIDE EFFECTS IN MALES

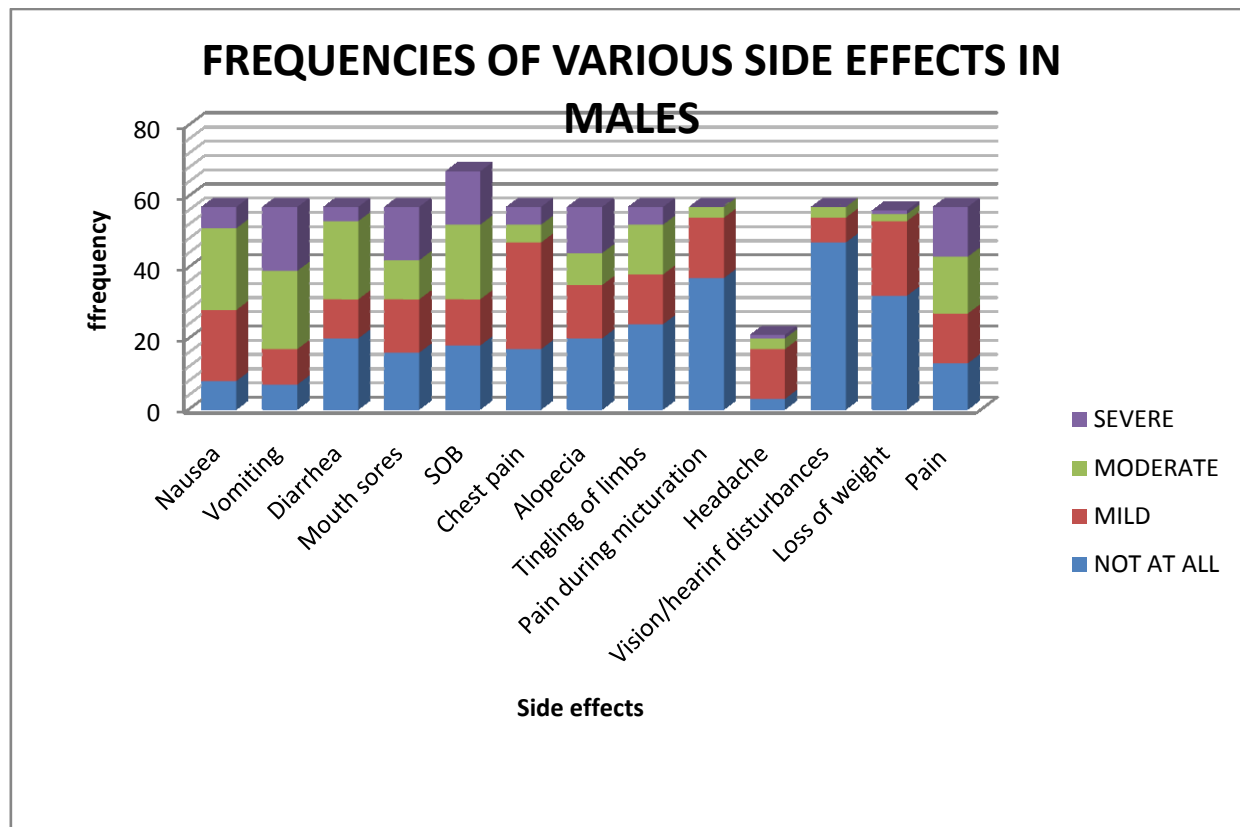


Fig.5: Frequencies of side effects in Males.

FREQUENCIES OF SIDE EFFECTS IN FEMALES

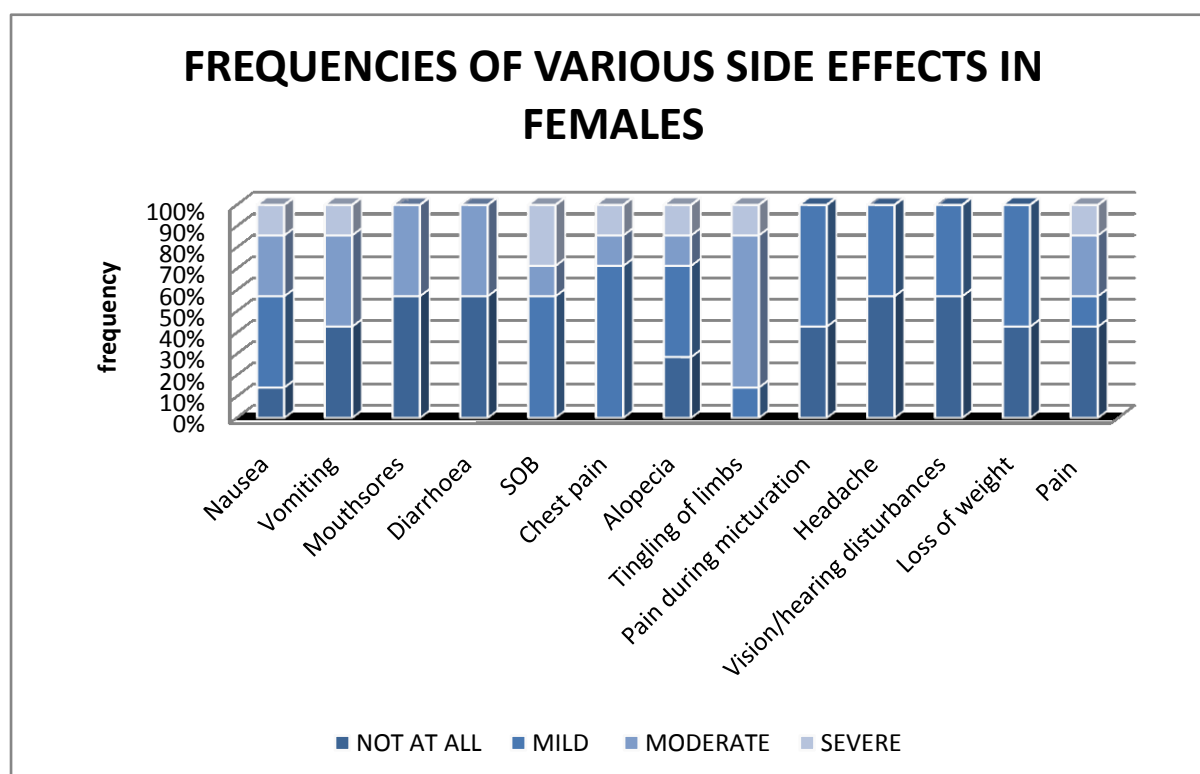
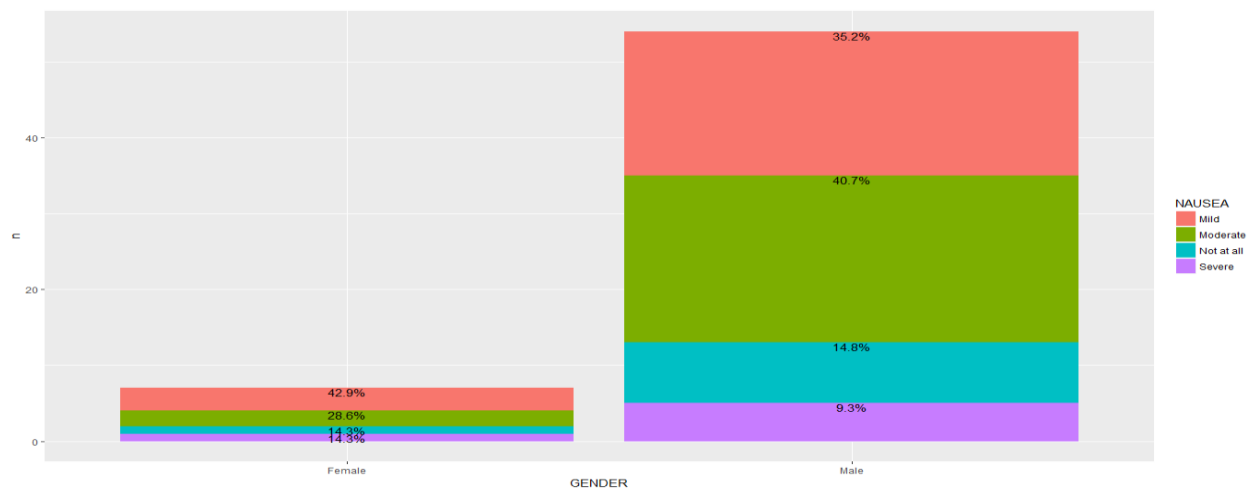
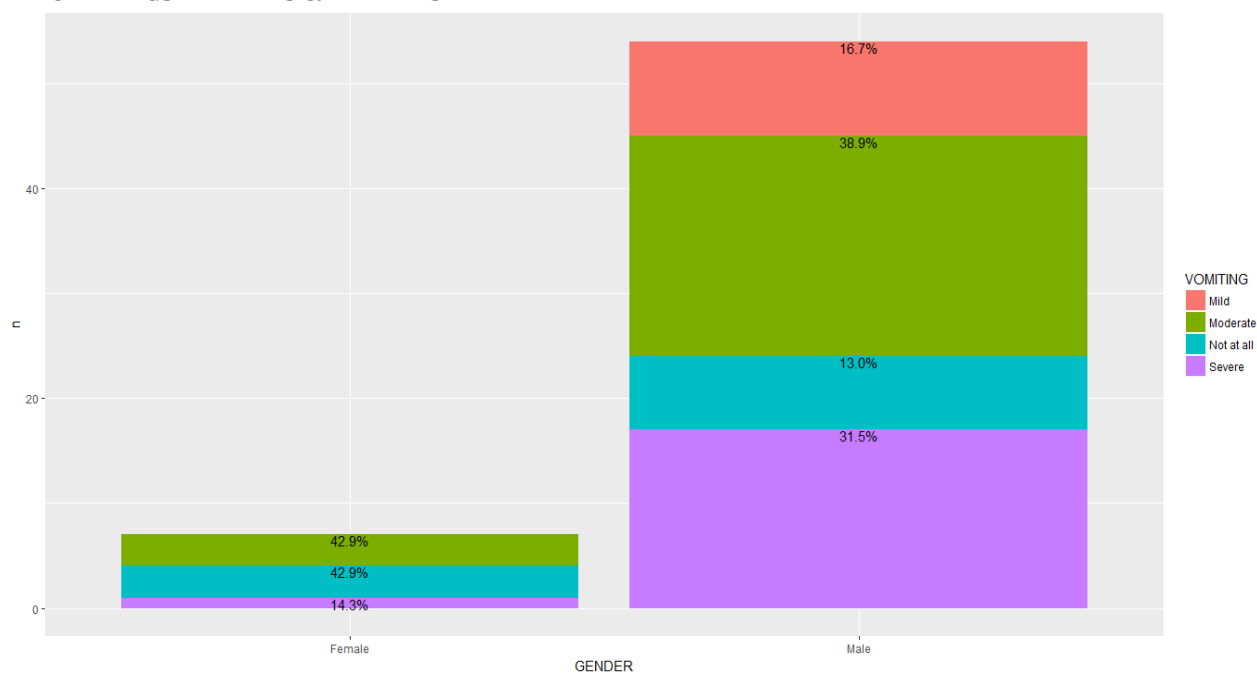
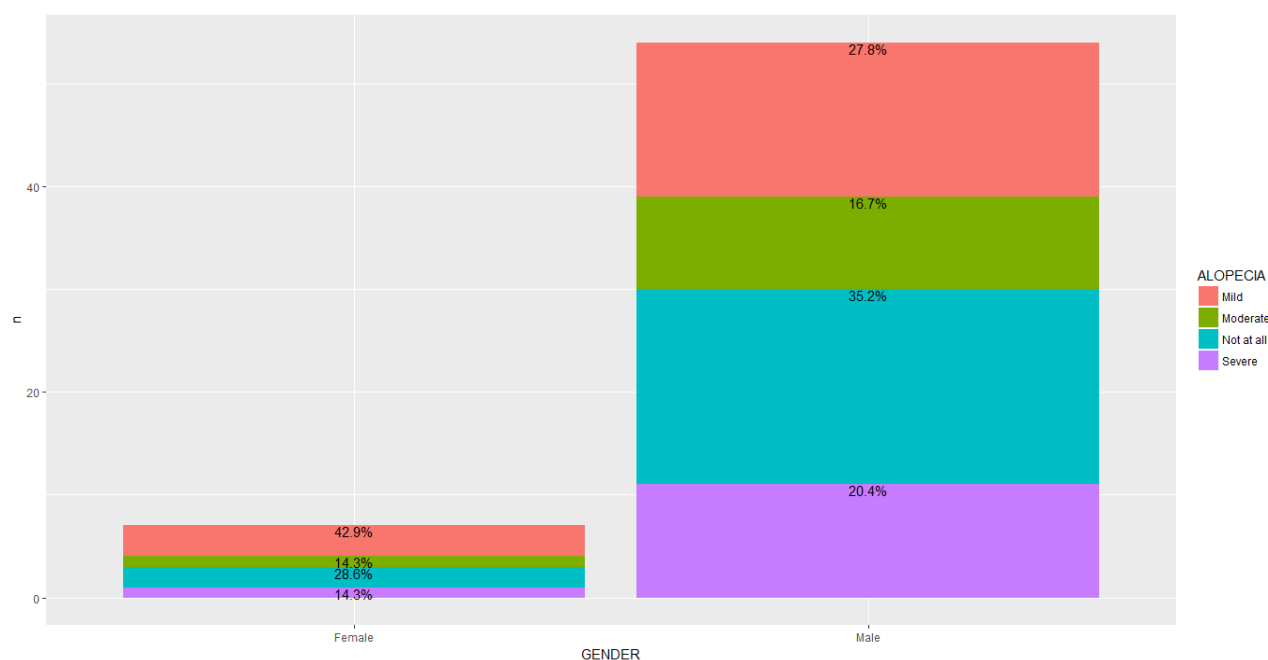
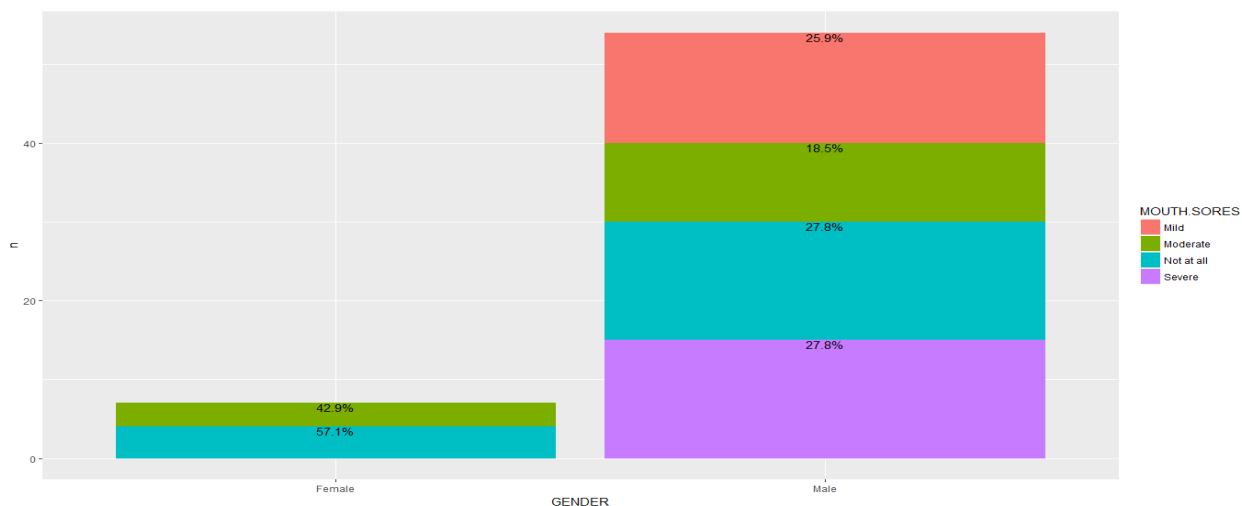
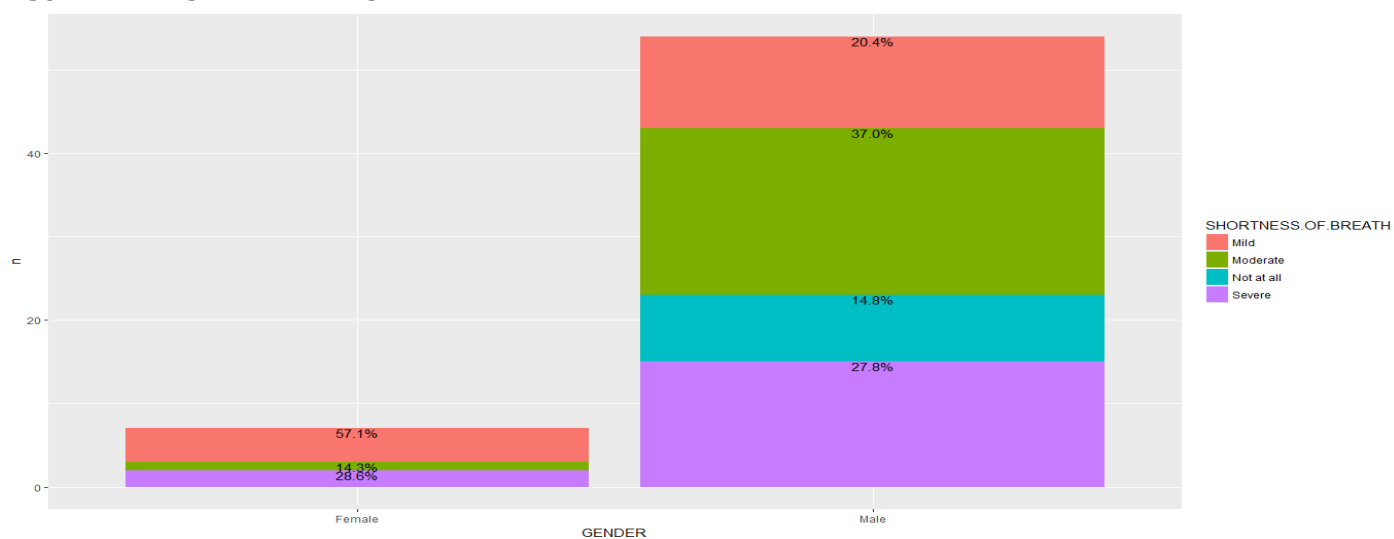
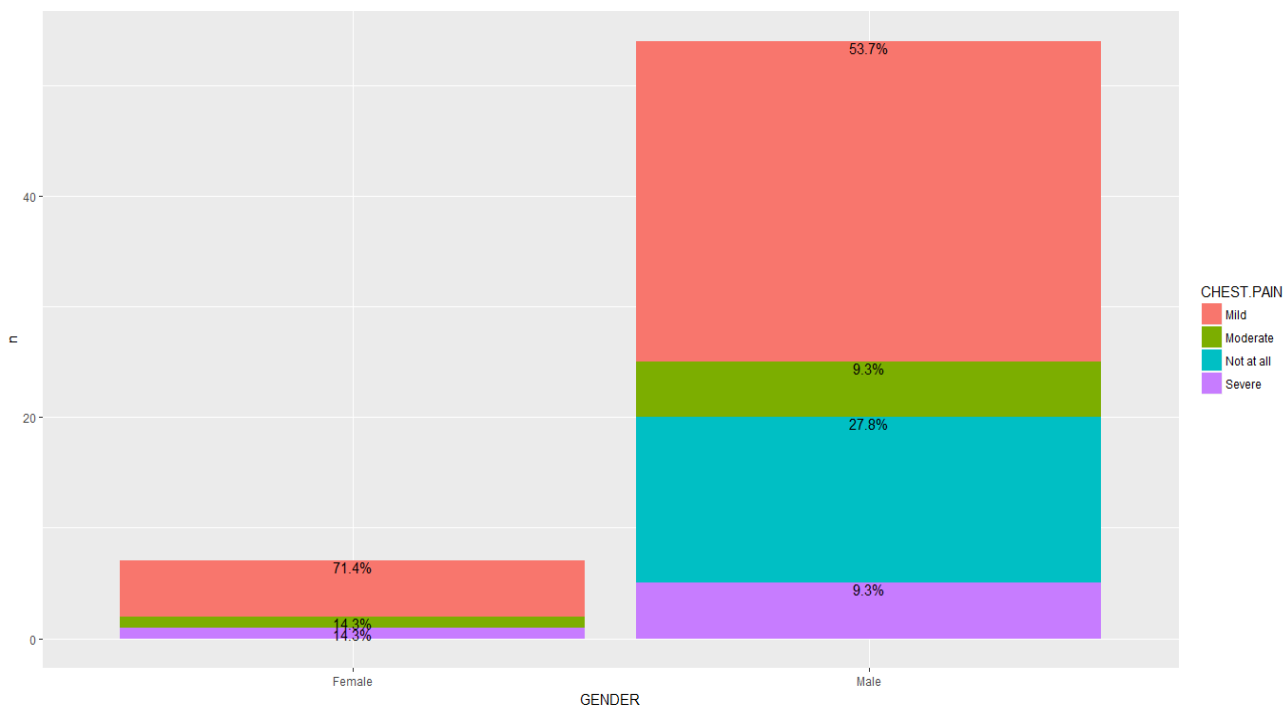
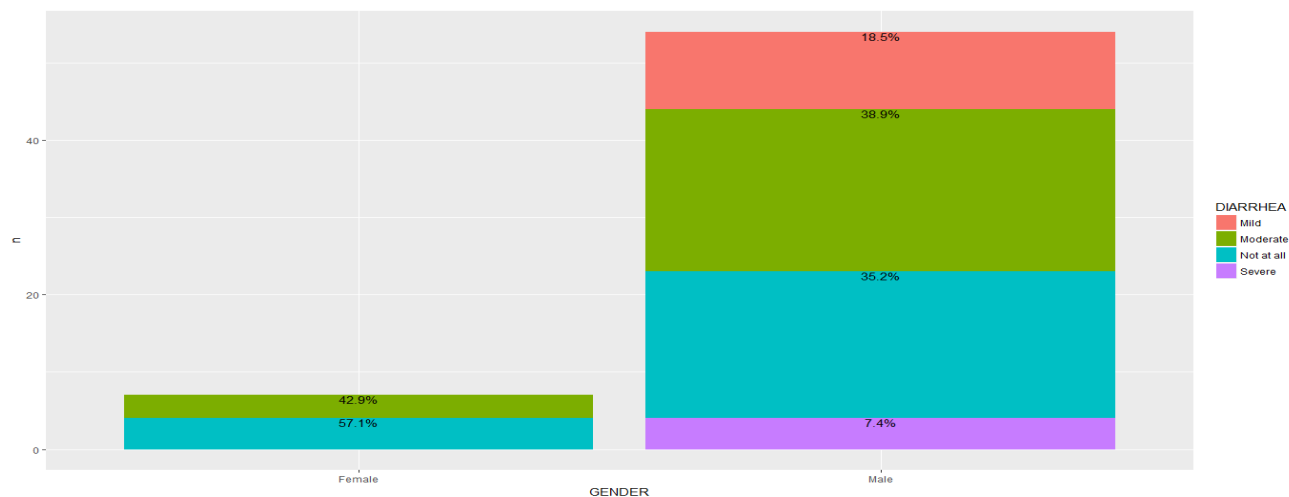
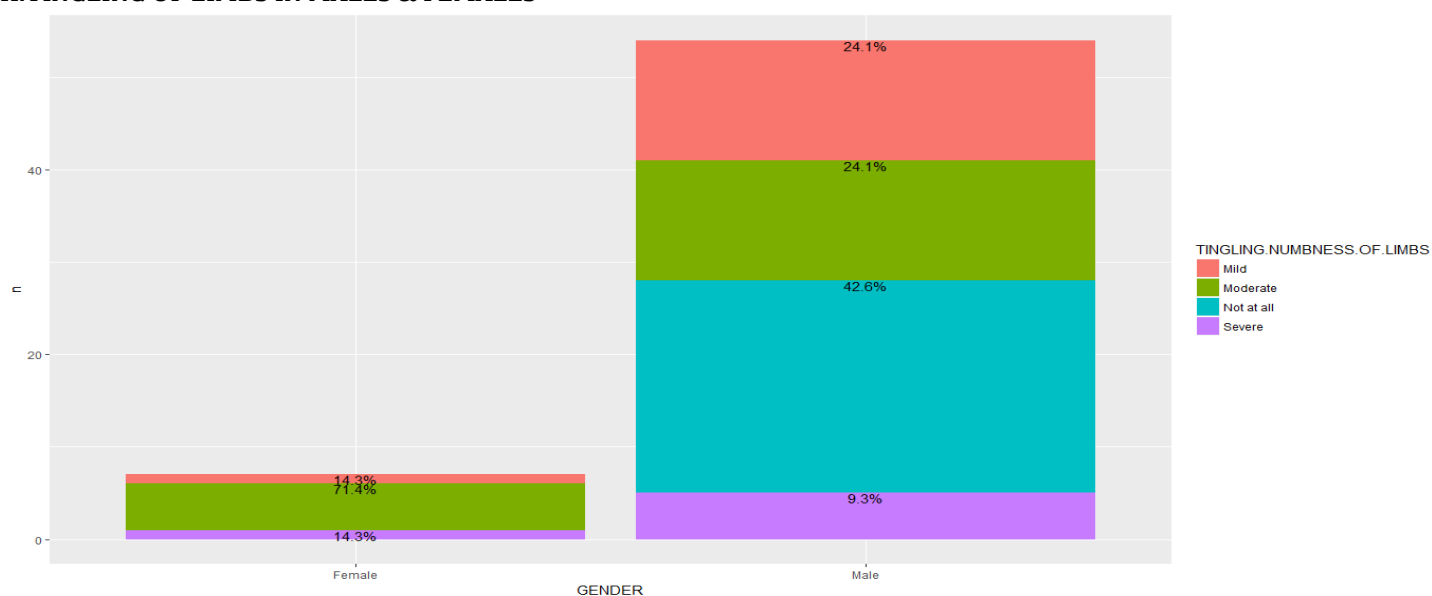
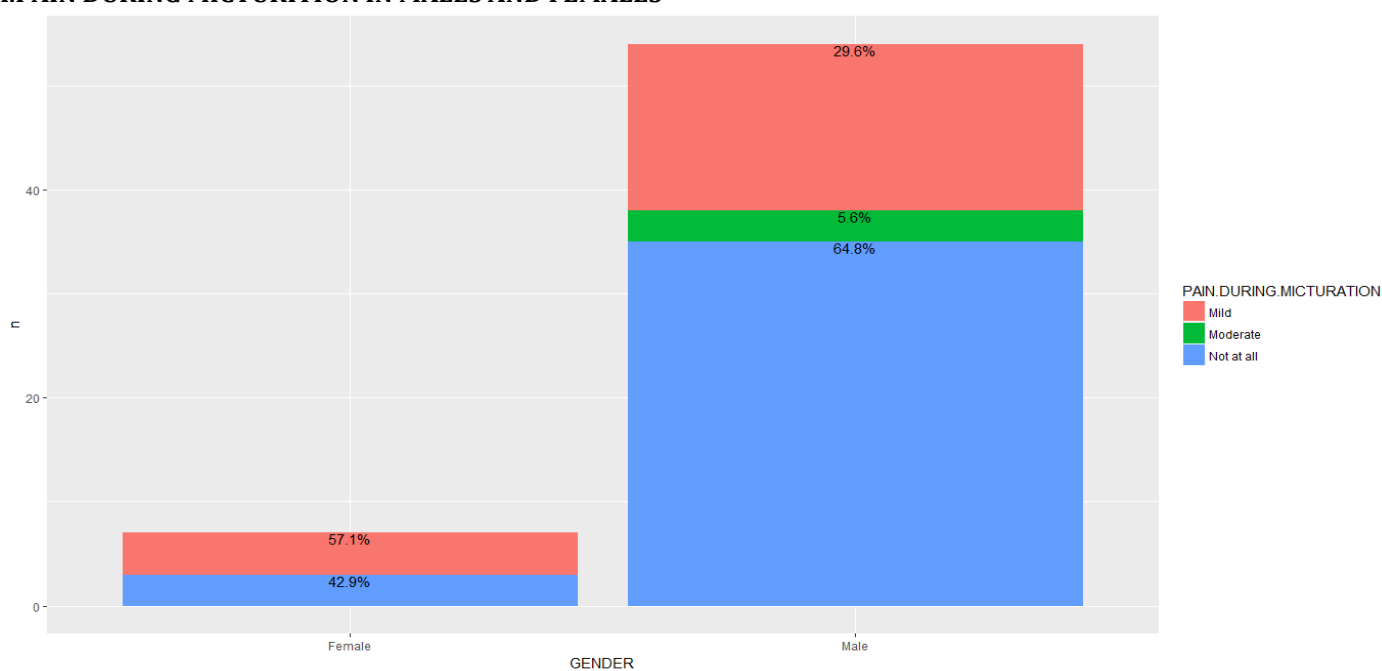
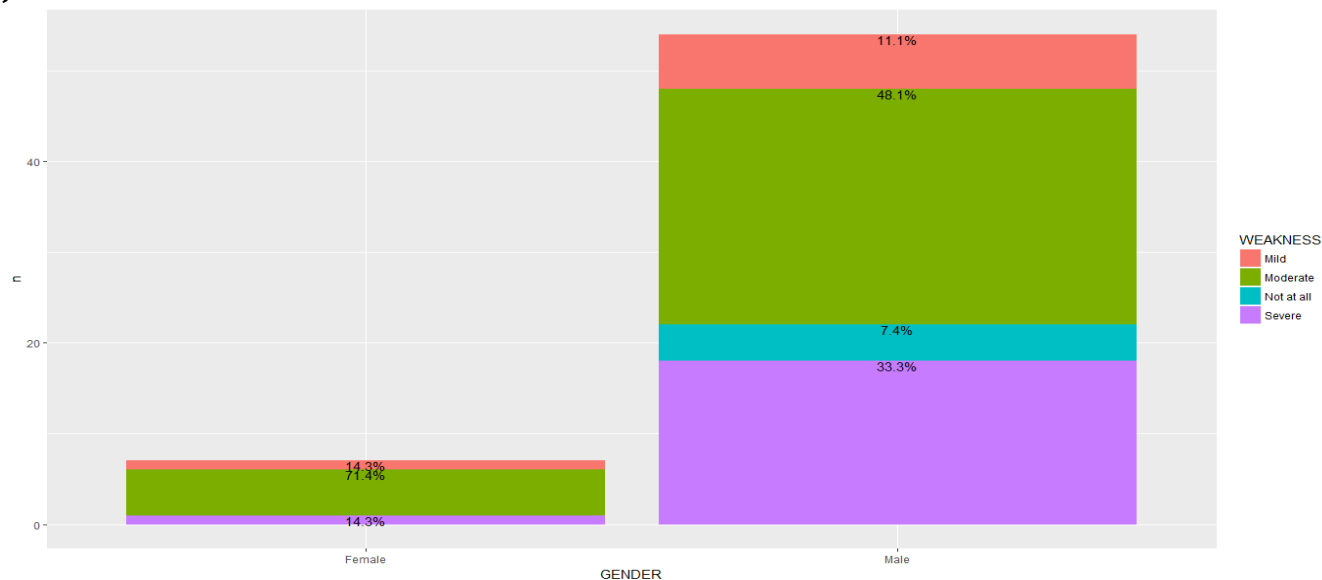
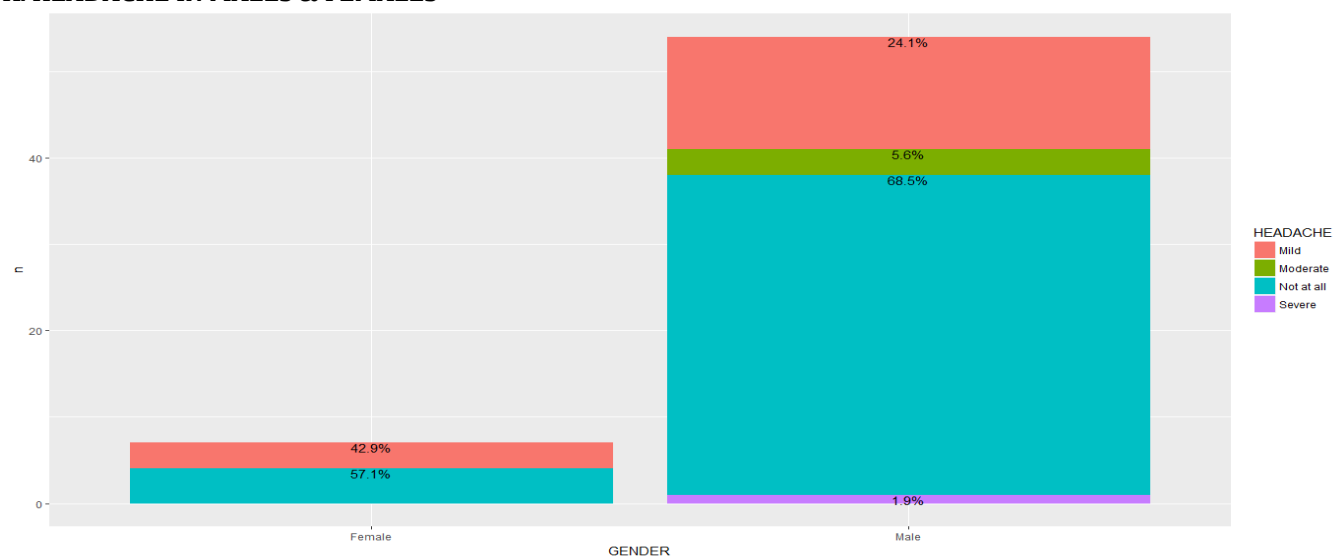
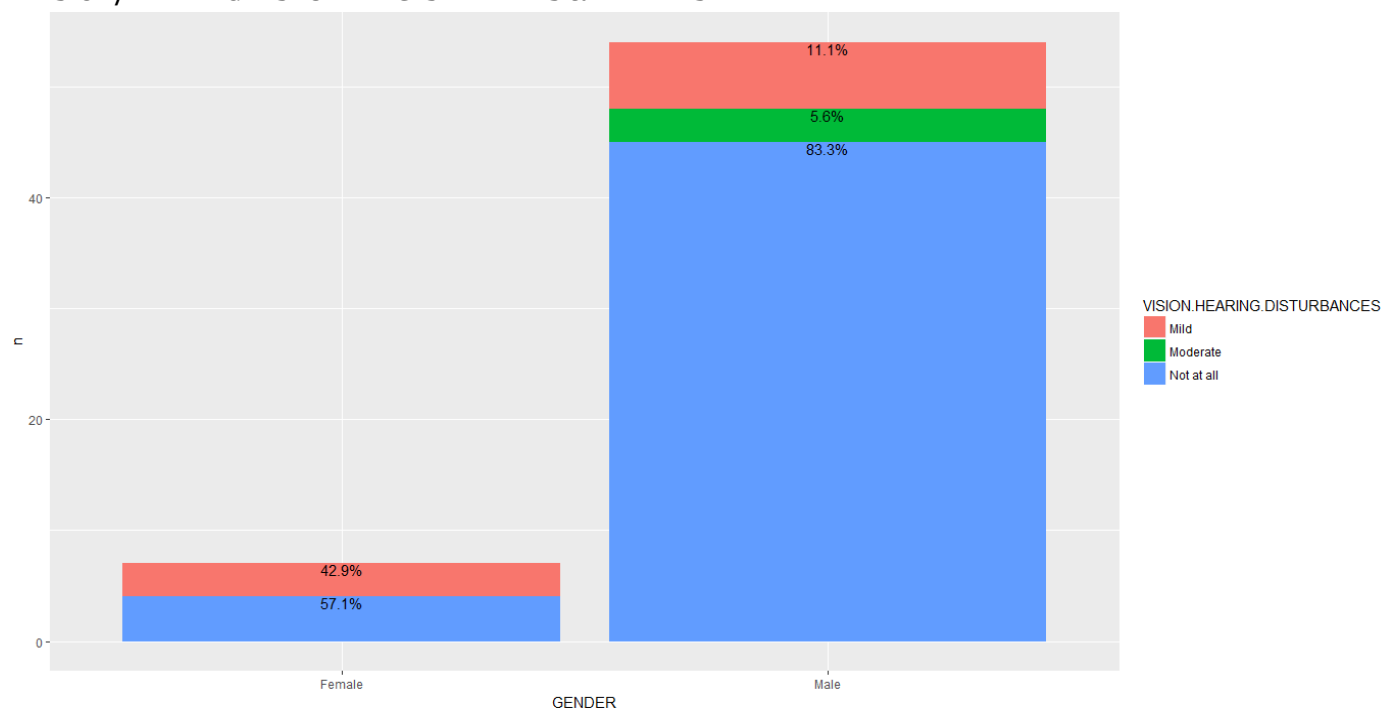


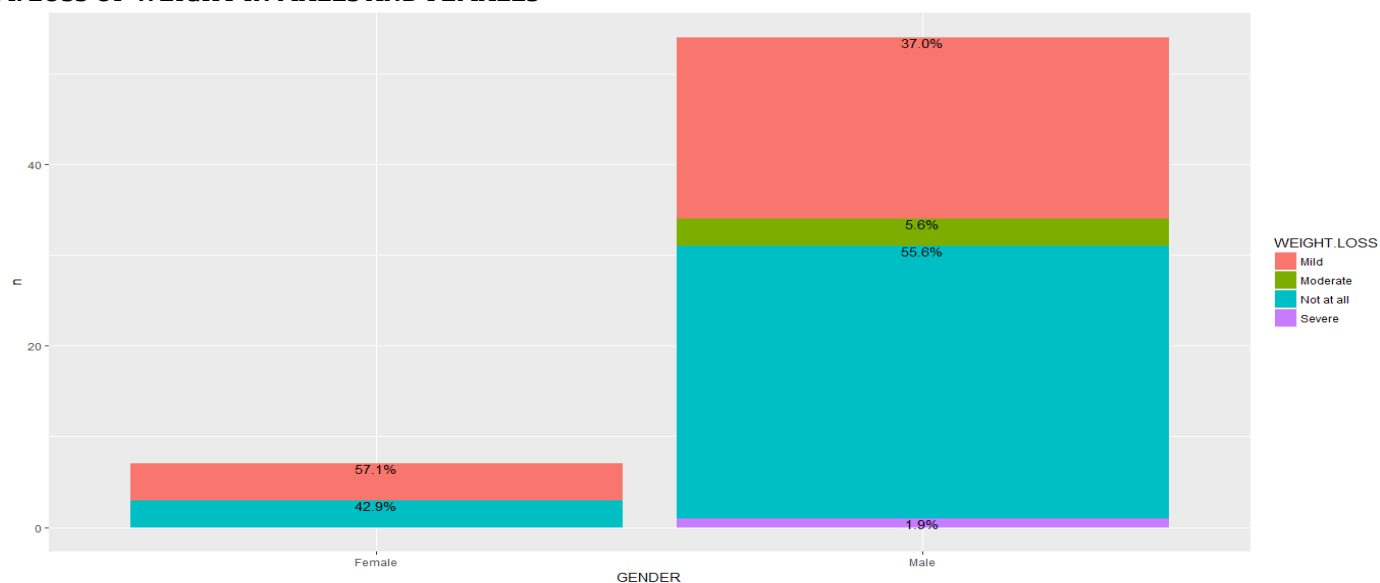
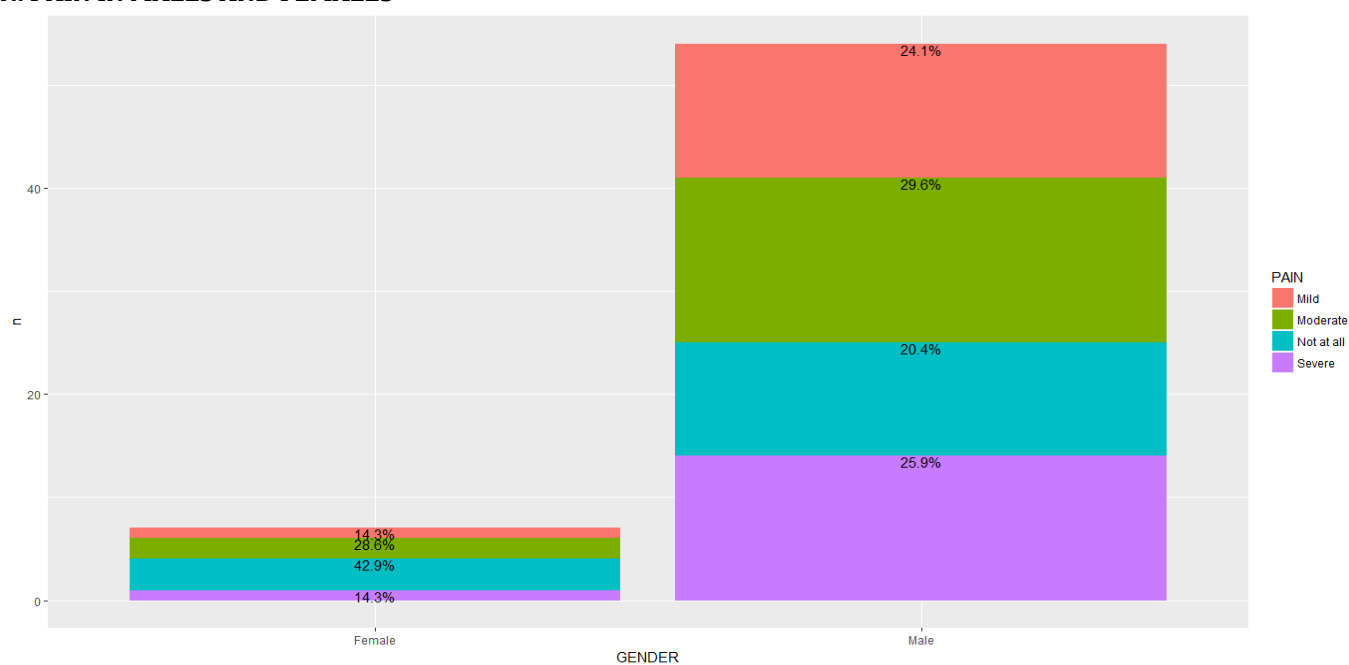
Fig.6: Frequencies of side effects in females.

A. NAUSEA IN MALES AND FEMALES**Fig.7: Nausea in males and females****B. VOMITINGS IN MALES & FEMALES****Fig.8: Vomiting's in males and females****C. ALOPECIA IN MALES AND FEMALES****Fig.9: Alopecia in males and females**

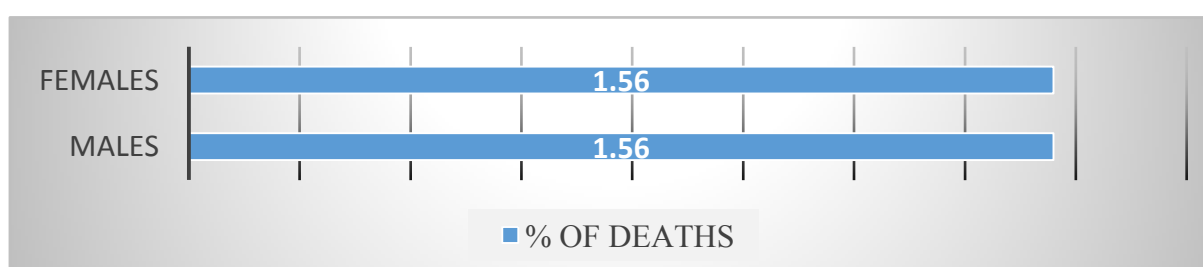
D. MOUTHSORES IN MALES AND FEMALES**Fig.10: Mouth sores in males and females****E. SOB IN MALES AND FEMALES****Fig.11: SOB in males and females****F. CHESTPAIN IN MALES AND FEMALES****Fig.12: Chest pain in males and females**

G.DIARRHEA IN MALES & FEMALES**Fig.13: Mouth sores in males and females****H.TINGLING OF LIMBS IN MALES & FEMALES****Fig.14: Tingling of limbs in males and females****I.PAIN DURING MICTURITION IN MALES AND FEMALES****Fig.15: Pain during micturition in males and females**

J. FATIGUE IN MALES AND FEMALES**Fig.16: Fatigue in males and females****K. HEADACHE IN MALES & FEMALES****Fig.17: Headache in males and females****L. VISION/HEARING DISTURBANCES IN MALES & FEMALES****Fig.18: Vision/hearing disturbances in males and females**

M. LOSS OF WEIGHT IN MALES AND FEMALES**Fig.19: Loss of weight in males and females****N. PAIN IN MALES AND FEMALES****Fig.20: Pain in males and females****7. MORTALITY RATE:****Table 8: Mortality rate**

GENDER	NO. OF PATIENTS EXPIRED	PERCENTAGE(%)
MALES	1	1.56
FEMALES	1	1.56
TOTAL	64	100

**Fig.21: Mortality rate**

8. DISTRIBUTION BASED ON FAMILY HISTORY

Table 9: Distribution based on family history

FAMILY HISTORY	NO. OF PATIENTS		PERCENTAGE (%)	
	MALES	FEMALES	MALES	FEMALES
PATIENTS WITH RELEVANT HISTORY	2	1	3.12	1.56
PATIENTS WITHOUT RELEVANT HISTORY	55	6	85.93	9.37
TOTAL NO. OF PATIENTS	64		100	

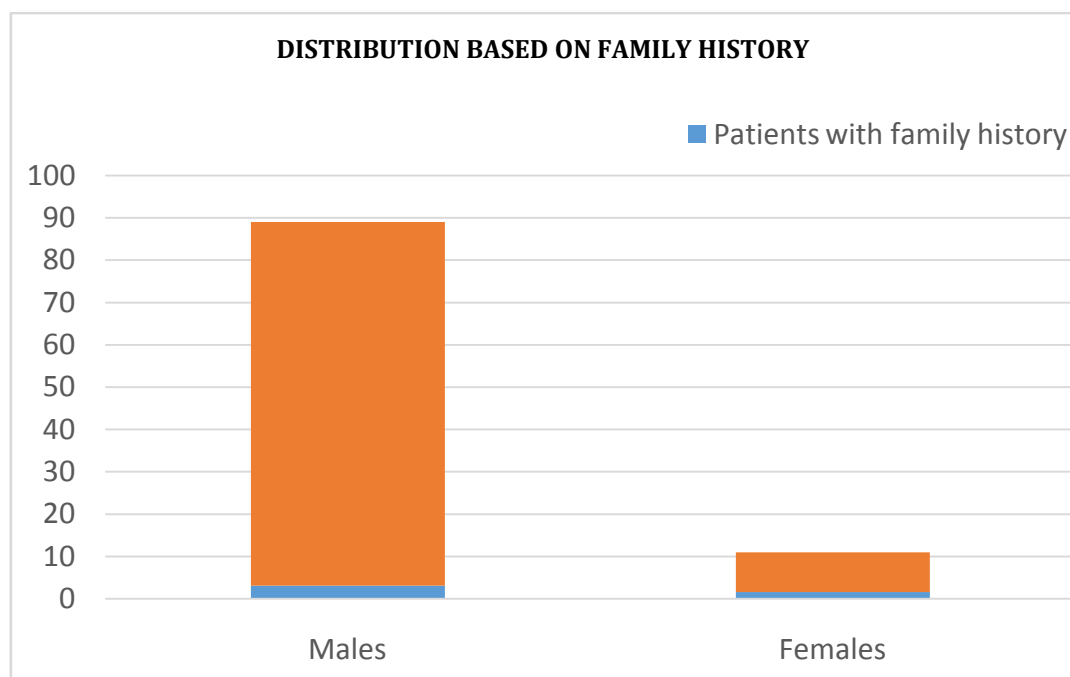


Fig.22: Distribution based on family history

CONCLUSION

We have conducted a prospective observational study including a total of 64 patients for a period of 6 months. Among 64 subjects undergoing CT for ALL, out of them ALL was dominantly diagnosed in males (89%). The incidence of ALL was also found more significantly in children of age group 0-14 years (33%), followed by it is the age group 15-24 years (18%). Of 64 patients studied, 57 patients experienced leukocytopenia, 38 experienced neutropenia, 46 experienced thrombocytopenia and anemia in 44 patients. Thus, increased rate of transfusions (45 in males, 5 in females) attributed to decreased quality of life of patients. 1 male and 1 female died during the study, due to SOB due to bilirubinemia and non-adherence to the CT. After analysis of collected data, it can be concluded that among various side effects associated with administration of VCR and ATC's, the most common side effects were nausea, vomiting, shortness of breath, chest pain, alopecia, mouth-sores. All of these side effects however are mostly reversible and last only for a particular period of time (up to a week) during the course of chemotherapy. Although encountering many side effects, with the administration of VCR and ATC's during the chemotherapy of acute lymphocytic leukemia, the patient's recovery is found to be effective, provided strictly adherent to all phases of chemotherapy. It can be concluded from the study that it requires detection and reporting of side effects and educating the patient regarding the side effects.

So, as to improve the patients' perceptions and management of side effects thus improving overall quality of life of patients.

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BIBLIOGRAPHY

1. What is cancer? <https://www.cancer.gov/about-cancer/understanding/what-is-cancer/>; Feb 9 2015
2. Cancer: Symptoms, Causes, Diagnosis, Classification and Management, <https://www.aimu.us/2016/10/20/cancer-symptoms-causes-diagnosis-classification-and-management/>; Oct 20 2016.
3. India against cancer statistics. <https://cancerindia.org.in/statistics/>; March 2, 2020.
4. Cancer. <https://www.mayoclinic.org/diseases-conditions/cancer/symptoms-causes/syc-20370588>.
5. Essentials of medical pharmacology. KD. Tripathi. Seventh edition.
6. Types of cancer treatment. <https://www.cancer.gov/about-cancer/treatment/types>.
7. Leukemia. <https://www.lls.org/leukemia>:
8. ALL. <https://www.leukaemia.org.au/blood-cancers/leukaemias/acute-lymphoblastic-leukaemia-all>; June 18, 2019
9. Vincristine and its side effects. <https://chemocare.com/chemotherapy/drug-info/vincristine.aspx>:
10. Anthracyclines. <https://chemoth.com/types/anthracyclines>: