Summer training at

PlasmaGen Biosciences, Bengaluru

(April 1 - May 31, 2019)

Usage Pattern Of IVIG In Oncology (Chronic Lymphocytic Leukaemia & Multiple Myeloma) and Rheumatology(Systemic Lupus Erythematosus and ANCA Vasculitis)

By

Vishalakchi

Under the guidance of

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MBA Pharmaceutical Management

2018-2020

School of Pharmaceutical Management

IIHMR Jaipur

2019

IIHMR UNIVERSITY

CERTIFICATE

This is to certify that **Vishalakchi** has undergone Summer Training at **PlasmaGen Biosciences, Bengaluru, India** from 1st April 2019 to 31st May 2019.

The candidate himself/herself completed the project assigned to him/her in Summer training. His/her approach to project was sincere and proactive. This Summer Training is in partial fulfillment of the course requirement recommended for the award of MBA in Hospital and Health Management/Pharmaceutical Management/Rural Management.

I wish him/her success in all his/her future endeavors.

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CERTIFICATE OF INTERNSHIP

THIS CERTIFICATE IS PRESENTED TO

Ms. Vishalakchi

In recognition to the valuable contribution towards the Marketing Research Project
in the field of Blood Plasma Products
on the topic

"USAGE PATTERN OF IVIG IN ONCOLOGY & RHEUMATOLOGY"

April, 2019 - May, 2019

Dr. Ranjeet S. Ajmani
Chief Executive Officer

PlasmaGen Biosciences

Acknowledgement

I am thankful for the completion of this summer internship work to the almighty god and my family who support and blessings were with me in every moment of my life.

I would like to extend my sincere gratitude to Dr.Ranjeet Ajmani (Chief Executive Officer), Mr.Awadhesh Tiwari and Ms. Payal, Marketing Team, PlasmaGen Biosciences for providing me an opportunity to learn and develop professionally. I thank for the freedom of thoughts expression and trust which was upon me. I would also like to pay my gratitude to entire team of Plasmagen Biosciences, Bengaluru who has helped me by sparing their valuable guidance to achieve my task successfully.

I would like to express my deep sense of gratitude to my academic mentor Dr.Sandeep Narula, Dean Pharmaceutical Management, IIHMR University, Jaipur Rajasthan .I am greatly thankful to him for providing his guidance at all stages of study the constructive suggestions and continuous encouragement help me to complete this project.

I am very much thankful to all the executive members and staff of PlasmaGen Biosciences for their support and cooperation.

I would like to thank all those who helped me directly and indirectly to complete this work.

At last but not the least most importantly I am thankful to God who is the creator and director of all the initial and final modes to reach the destiny.

Vishalakchi

MBA. Pharmaceutical Management

(10^{th} Batch)

Declaration

I hereby declare that this Summer Internship project in PlasmaGen Biosciences Bengaluru submitted to IIHMR University Jaipur in the partial fulfilment of requirement for the award of degree of MBA Pharmaceutical management is a Bonafide and the study carried out by me under the guidance of **Dr Sandeep Narula** Dean Pharmaceutical Management IIHMR University Jaipur . The extent of information gathered in the study is discussed in this project report. This work is original and confidential.

VISHALAKCHI

CONTENT TABLE

Executive Summary

This is a study accomplished in PlasmaGen Biosciences in targeted cities of country. The purpose was to find out usage pattern of IVIG in Oncology (Chronic Lymphocytic Leukaemia and Multiple Myeloma) and Rheumatology (Systemic Lupus Erythematosus and ANCA Vasculitis). Study conducted in various location like Chennai, Hyderabad and Mumbai. In these locations by the study it was ensured that whether IVIG usage was done or not if not then what was the reason behind it. and various feedback were collected from the super speciality division.

My first step involves the detailed study of various disease related to this project then in next part of the study identification of the location was done and accordingly the survey questionnaire has been prepared. With the help of survey questionnaire desired data were obtained as per my objectives of project. Data analysis was accomplished by considering different aspect of the study. Findings were made through data collected and prevalence of disease were found in different location with varying age groups and the line of treatment which was extensively used. Thus, as compared rheumatologist, oncologists were not supportive towards IVIG due to various standard regimens, regulatories and affordability.

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Company profile

"PlasmaGen Biosciences is an Indian biopharmaceutical organization specializing in Plasma Protein Therapy, pursuing a vision of ushering the plasma protein in India and SAARC Nations. PlasmaGen Biosciences was established in the year 2010 on September 7th.The widest range of immunoglobulins in India catering to the requisites of various realms viz. Haematology, Oncology, Immunology, Paediatrics, Rheumatology, Dermatology and Neurology."

PHILOSOPHY:

"Aims to provide a wide range of safe plasma products to improve the health and quality of life of patients."

MISSION:

- Provide a wide range of safe plasma products to patients, in India and SAARC (South Asian Association for Regional Cooperation) region, on consistent basis.
- Create strategic partnership to enable the global market accessible to India and SAARC region.
- Develop a consortium of stakeholders involved in Plasma Protein Therapy to optimize the use of surplus unutilized plasma for India and SAARC region.
- Pave the road for achieving self-sufficiency in Plasma Protein Therapy in India and SAARC region.
- Work in close association with regulatory agencies and collaborate with research institutions to change the landscape of Plasma Protein Industry in India.

VISION:

To achieve global recognition and trust, as an Indian plasma product company, dedicated towards improving the health and quality of life of patients in India and SAARC (South Asian Association for Regional Cooperation) region.

VALUES:

1.Leadership- Courage and passion

2.Respect and Integrity- Transparent work environment

3.Quality- Reflection of our excellence

4.Social responsibility- People and environment

5.Harmony- work- life balance

6.Customer satisfaction- Exceeded expectation

BLOCKBUSTER PRODUTS:

1.PlasmaGlob

2.AlbuMax

3.PlasmaRho- D.I.V

4.PlasmaRho-I.M

5.PlasmaRab

6.PlasmaHep

7.VerBumin

8.GammaFact- VIII

QUALITY AND SAFETY

For us, Quality is an attitude or rather a way of life that we endeavour to lead without any placation. Our attempt is to ensure that each step and every person involved at each level, lines in congruence with the same standards of quality as necessitated by this realm. When it comes to procurement, management, fractionation of plasma & manufacturing plasma products; we lay immense exertion on efforts to ensure safety at all levels .All the blood banks that we collect plasma from are licensed by the concerned regulatory authority and undergo extensive audits by us to ensure safe supply of plasma.

Introduction

Intravenous immunoglobulin (IVIG) enhances immune homeostasis by modulating expression and function of Fc receptors, interfering with activation of complement and production of cytokines, providing anti-idiotypic antibodies, and affecting the activation and effector functions of T and B cells. These mechanisms may explain the effectiveness of IVIG in autoimmune neuromuscular disorders. **Immunoglobulin therapy**, also known as **normal human immunoglobulin** (**NHIG**), is the use of a mixture of antibodies(immunoglobulins) to treat, these conditions include primary immunodeficiency, immune thrombocytopenic purpura, chronic inflammatory demyelinating polyneuropathy, Kawasaki disease, certain cases of HIV/AID Sand measles, Guillain-Barré syndrome. Immunoglobulin therapy is used in a variety of conditions, many of which involve decreased or abolished antibody production capabilities, which range from a complete absence of multiple types of antibodies, to IgG subclass deficiencies (usually involving IgG2 or IgG3), to other disorders in which antibodies are within a normal quantitative range, but lacking in quality - unable to respond to antigens as they normally should – resulting in an increased rate or increased severity of infections.

Thus, the project flow involves the usage pattern IVIG in different autoimmune disorder. IVIG could be used as lifelong treatment through escalating dose and could be used for multiple diseases. In this we are dealing with Chronic Lymphocytic Leukaemia, Multiple Myeloma, Systemic Lupus Erythematosus and ANCA Vasculitis.

Leukaemia: a malignant progressive disease in which the bone marrow and other blood forming organs produce increased number of immature or abnormal leucocytes. These suppress the production of normal blood cells leading to anaemia and other symptoms.

Chronic Lymphocytic Leukaemia- is a type of cancer of blood and bone marrow. It typically progresses more slowly than other types of leukaemia.

Multiple Myeloma- A bone marrow cancer that involves a type WBC called a plasma (Myeloma) cell. The tumour cell in myeloma can form a single collection (Plasmacytoma) or many tumours (Multiple Myeloma) Plasma cells are normally part of the immune system they make antibodies,because myeloma patients have an excess of identical plasma cells they have too much of one type of antibody.

Different prognostic parameter importance:

1.Lymphocytosis

2.Lymph node enlargement

3. Hepatomegaly and splenomegaly.

4. Anaemia and Thrombocytopenia

In any stages the complications lies down thus IVIG gives antibodies that your body is not making on its own so that one could fight against the infections.

Systemic Lupus Erythematosus- a chronic inflammatory variable autoimmune disease of connective tissue that occurs chiefly in women and typically characterized by fever, skin rash, fatigue. It is multisystem autoimmune disorder. In this butterfly shaped cheek rash has

been found, small sores, develop arthritis, joints become inflamed and swollen. Fingers are cold they may turn to blue or white colour this is called Raynaud's Phenomenon. Disease affects skin by affecting multiple organs by reddening of skin, looks like wolf bite.

ANCA Vasculitis- It is a rare disorder affecting many organs of body by attacking the blood vessel. most often the small blood vessel.

Adverse reactions associated with use of IVIG include minor, self-limited reactions, such as headache, chills, myalgia, low back pain, or chest discomfort, that occur early in the infusion but dissipate after the infusion rate is slowed moderate but rare and inconsequential incidences of aseptic meningitis, especially in patients with a history of migraine, and dermatologic reactions, including urticaria, lichenoid lesions, palmar pruritus, or petechiae, that develop up to 5 days after infusion and more serious but rare reactions, including anaphylaxis in patients with a severe deficiency of IgA when they have anti-IgA antibodies, acute but often reversible renal tubular necrosis in patients with pre-existing kidney disease and volume depletion, and thromboembolic events, such as stroke, myocardial infarction, or pulmonary embolism due to IVIG-associated increased plasma viscosity in patents at increased risk for thrombosis, such as elderly, diabetic, thrombocytosis, or hypergammaglobulinemic patients.

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Rationale

IVIG is considered to increase antibodies that patient body is not making on its own so that one could fight against the infections. In these conditions patient do die due to the infection rather than the disease itself. Intravenous immunoglobulin is used in the treatment of a wide range of immunologic diseases that affect the entire neuraxins, including brain, spinal cord, peripheral nerves, neuromuscular junction, and muscles. Based on controlled clinical trials, IVIG is the treatment of choice for Guillain-Barré syndrome, multifocal motor neuropathy, and CIDP and is useful instead of plasma exchange in myasthenia gravis management; IVIG is also effective in aggressive or treatment-resistant dermatomyositis and improves function in patients with stiff-person syndrome. Occasionally, patients with inclusion body myositis may derive modest but transient benefit, especially in dysphagia, but most do not respond. However, IVIG cannot reverse established weakness or chronic optic neuritis in patients with MS. The efficacy of IVIG in relapsing-remitting MS is unsettled and currently under investigation in a large controlled trial.

The aim of the study was to find out the usage pattern of IVIG in oncology department to know the understandings and awareness of IVIG amongst targeted doctors, probing the doctors and also recognising the ground level problems faced when interacting doctor.

The project has been done through targeting the cities once versed by the several diseases through doing surveys and come up with the ideas to improve the present scenario

Objectives

MAIN OBJECTIVE:

- To identify usage pattern of IVIG in Oncology and Rheumatology.

SUB-OBJECTIVE

- Prevalence of disease among different cities in various super speciality division.
- To find out the rare age group.
- To analyze data variation in different cities for the usage of supportive therapy and IVIG Usage.
- To find out whether doctor use IVIG or not with its appropriate reason and attributing factors.

Methodology

Study area – Bangalore, Chennai, Hyderabad and Mumbai.

Type of study – Descriptive Study(Cross Sectional)

Sample Size- 57(For CLL and MM)

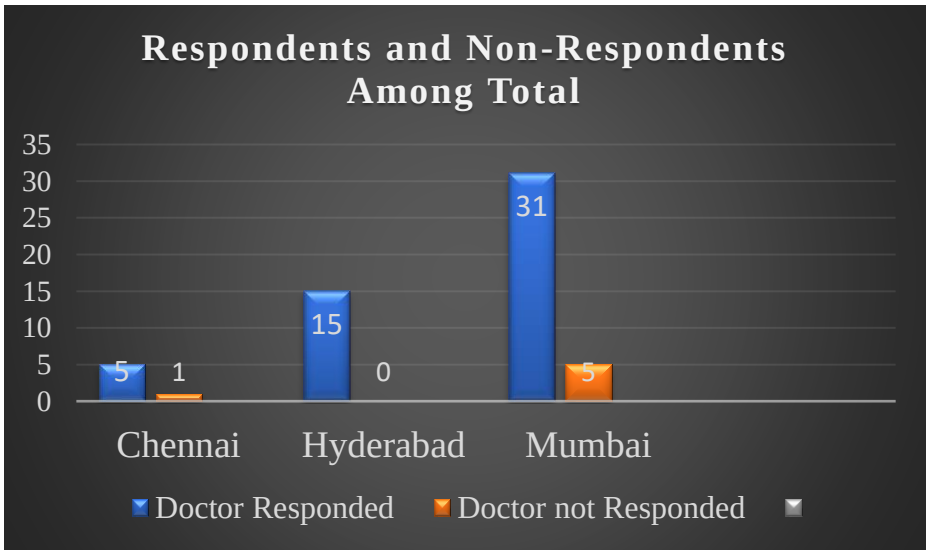
Sample Size- 22(For SLE and ANCA Vasculitis

Data collection method

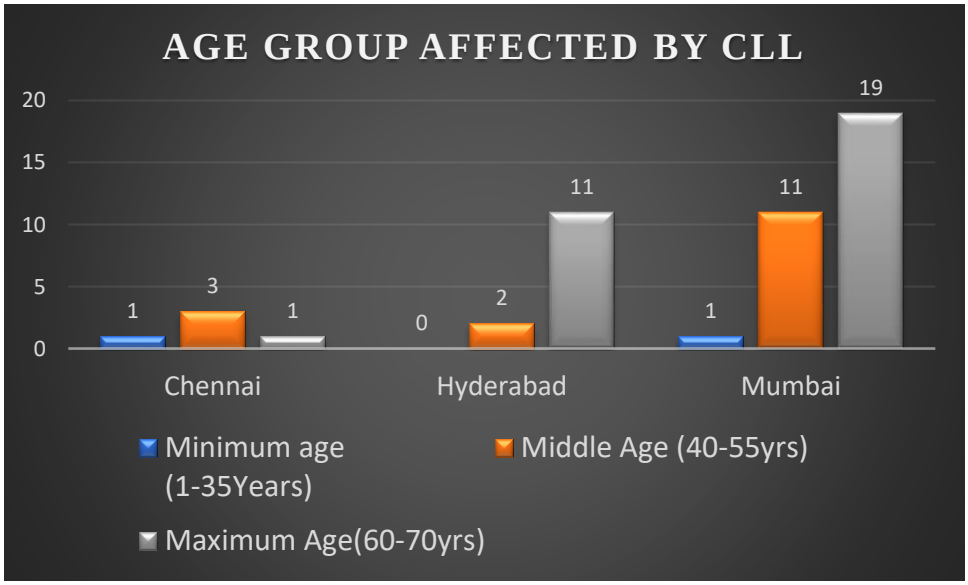
Primary – Survey

Findings and data analysis

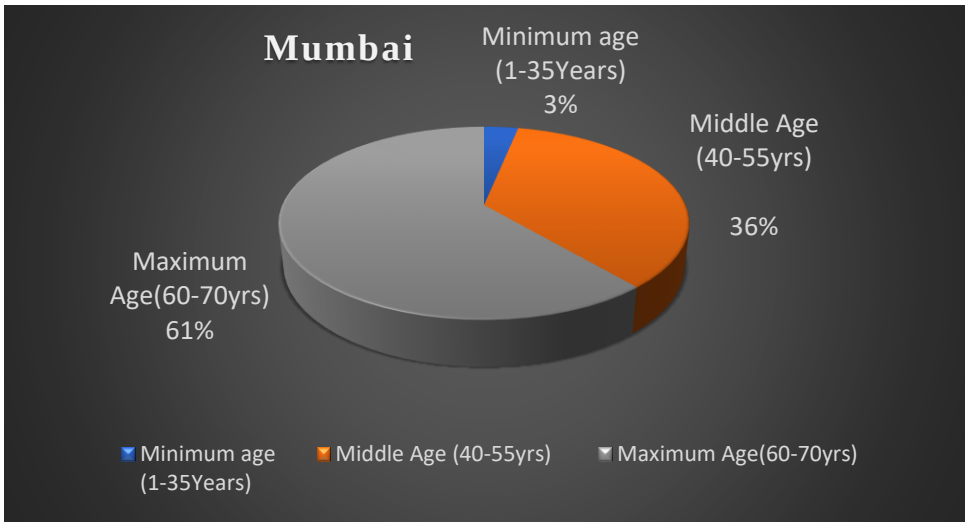
FOR CHRONIC LYMPHOCYTIC LEUKAEMIA AND MULTIPLE MYELOMA:



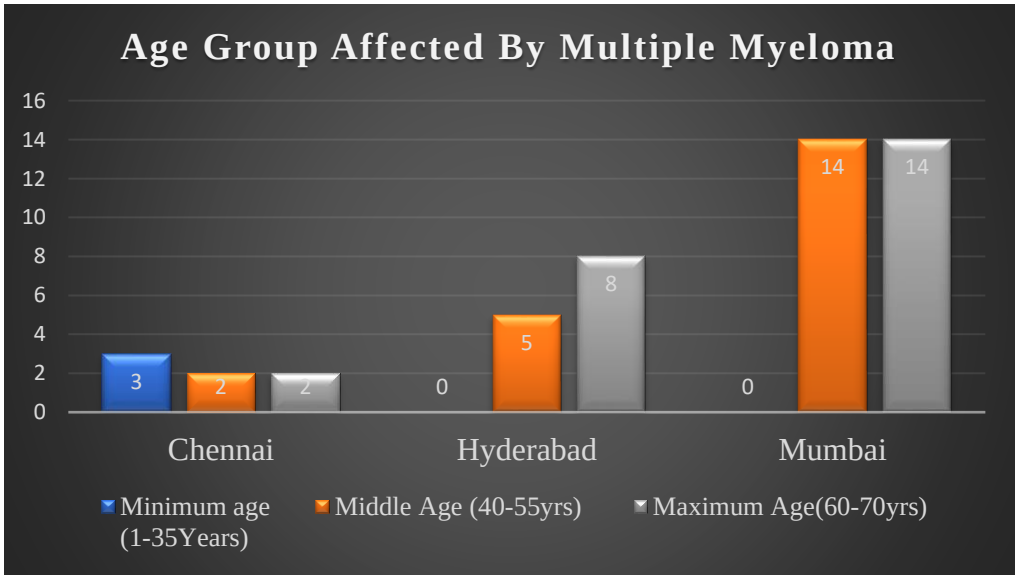
Interpretation-The above bar graph shows the no. of respondents among different cities in which Mumbai is in high as the usage was highest in Mumbai i.e 31 doctors of super speciality division who deals with rare disorders do interacted as shared few information regarding the CLL and MM.



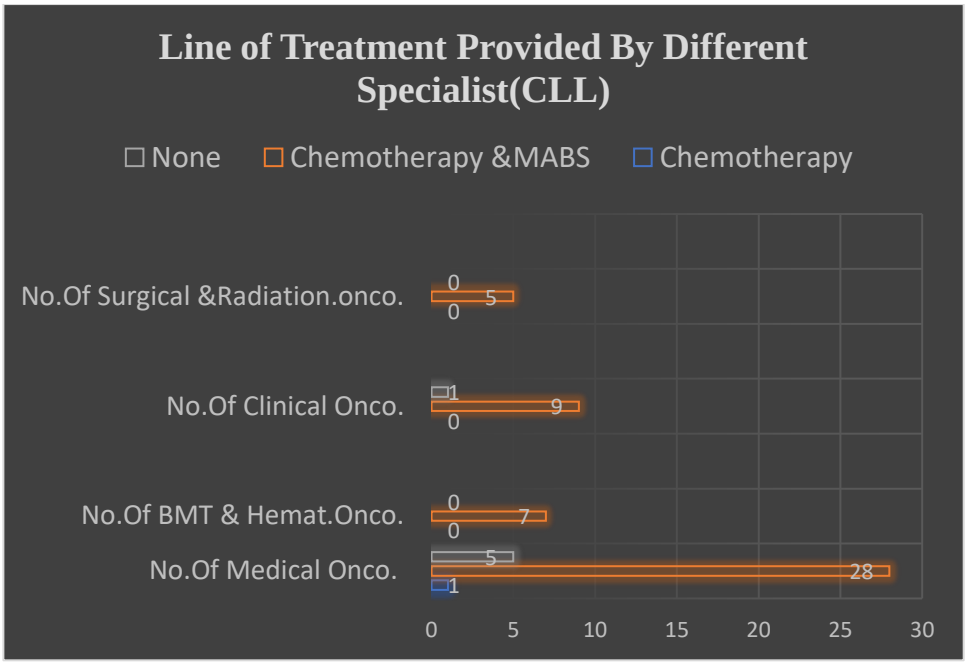
Interpretation- Generally it's been considered that the age group that is susceptible to these disease are from 60 to 70yrs but according to the respondents information it has been found that middle age is suffering the most and one or two cases has been also seen from age group which is 34ys considered to be rare of the rarest.



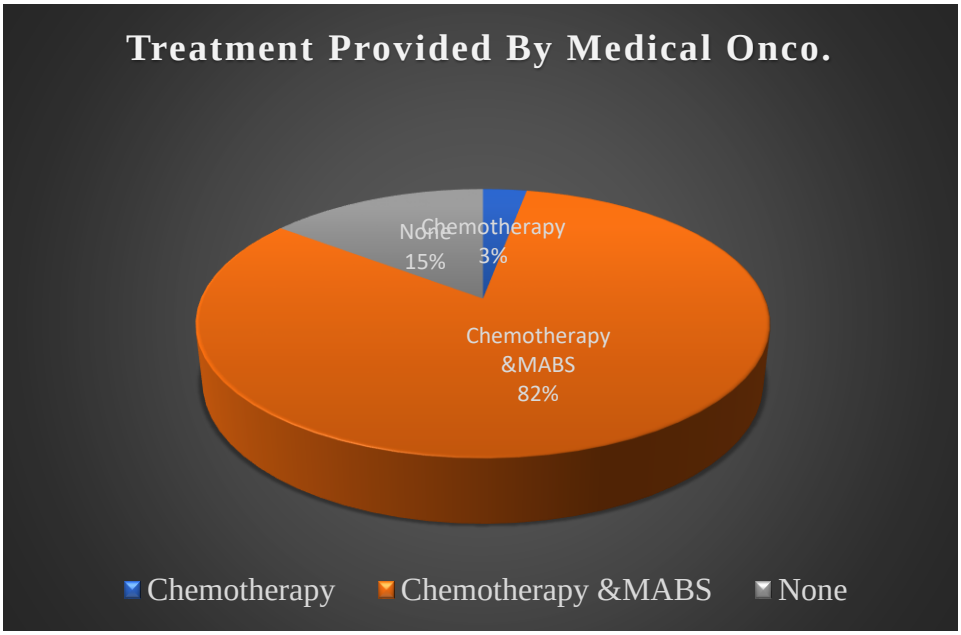
Interpretation- As compared to all three cities the middle age and maximum age patient are found to be highest in Mumbai as the doctors were aware about the IVIG and its usage. In other cities it was less as the doctors considered that it's not a standard regimen and also the affordability was one of the parameter.



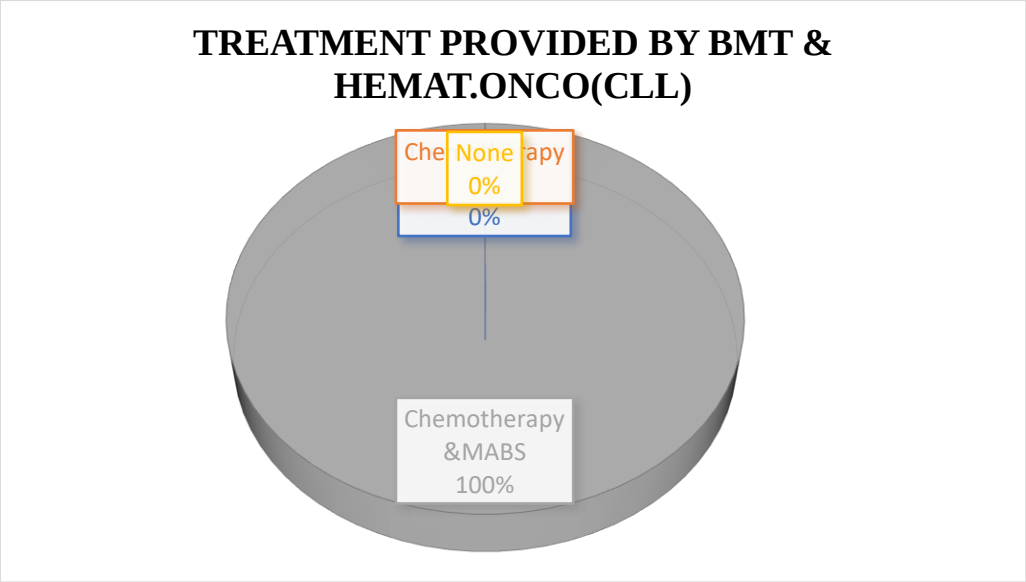
Interpretation-According to the respondents the age group affected the most by Multiple Myeloma was middle age and maximum age which was found to be highest in Mumbai. Thus, according to the respondents of Hyderabad and Chennai doctors were not encountering the patient so they were unable to provide information regarding this.



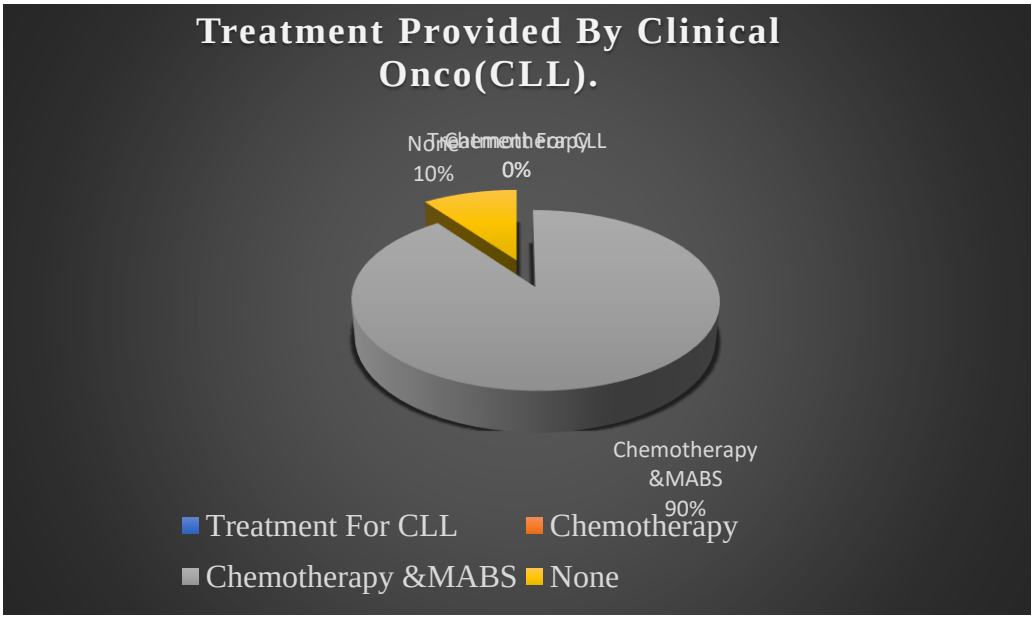
Interpretation- The above graph shows that how the line of treatment varies according to different specialities considering all three cities i.e. Chennai, Hyderabad, Mumbai. According to the different specialities chemotherapy and MABS are used the most in which majorly Medical oncologist are incorporating this line of treatment at high. The reason behind using chemotherapy and MABS was its synergistic effect.



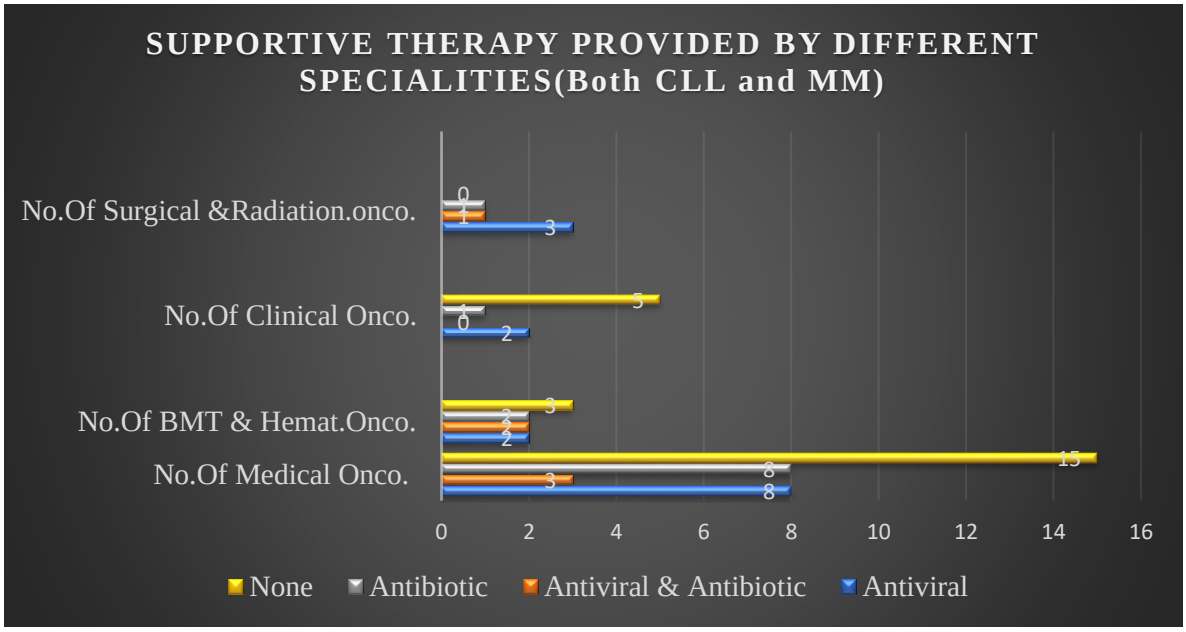
Interpretation-According to the respondents it has been found that 82% of the medical oncologist from three cities are incorporating chemotherapy and MABS rather than going for only Chemotherapy. 8% of medical oncologist go for only chemotherapy. Rest 15% of the doctors did not respond due to the heavy OPD schedule.



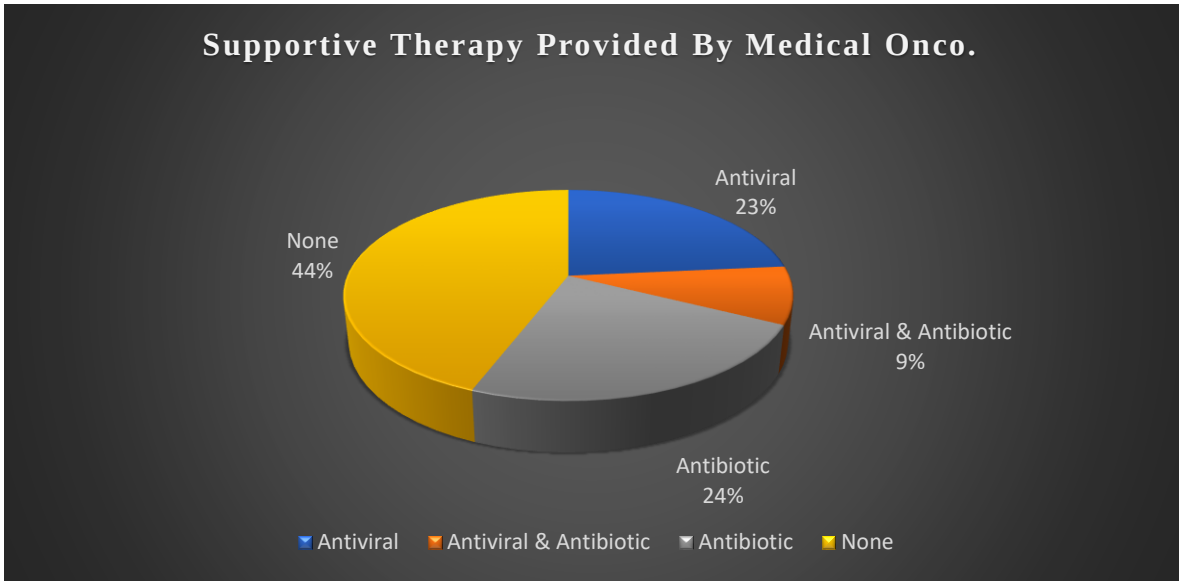
Interpretation- According to the data provided by the respondents all of them incorporate chemotherapy and MABS as the first line treatment for the CLL. The reason behind incorporating is that the action is quite rapid and also shows synergistic effect.



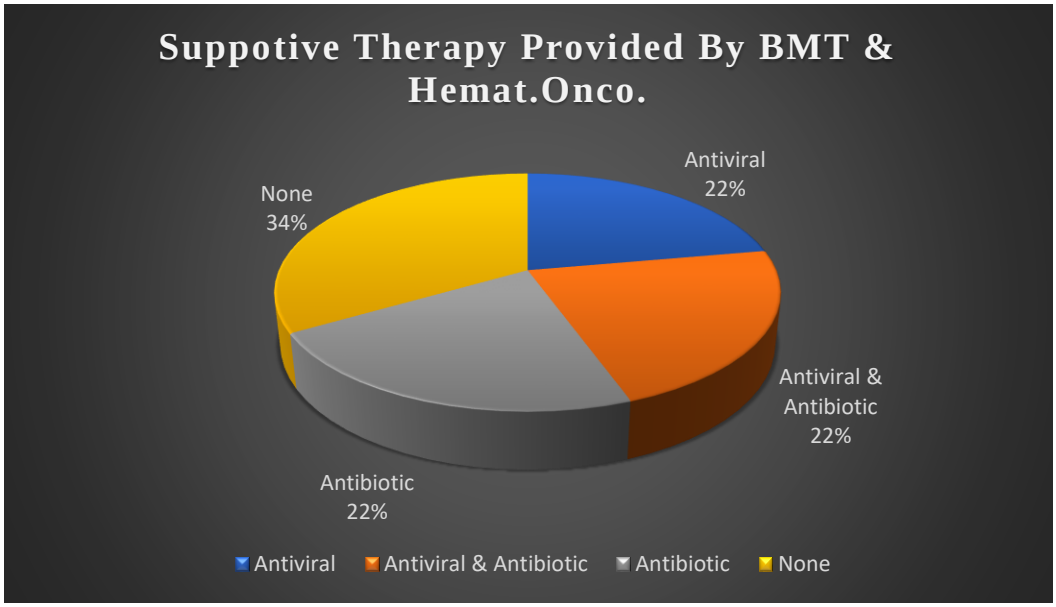
Interpretation-According to the above graph it has been found that 90% of Clinical Oncologist incorporate Chemotherapy and MABS and the rest 10% are the clinical oncologist who did not responded, as they don't provide any data or interacted .One of the reason behind incorporating chemotherapy and MABS is that it acta as destruction of the of monoclonal bodies which is formed due to abnormal myeloma cells which is responsible to produce monoclonal bodies ,thus, they imply the same.



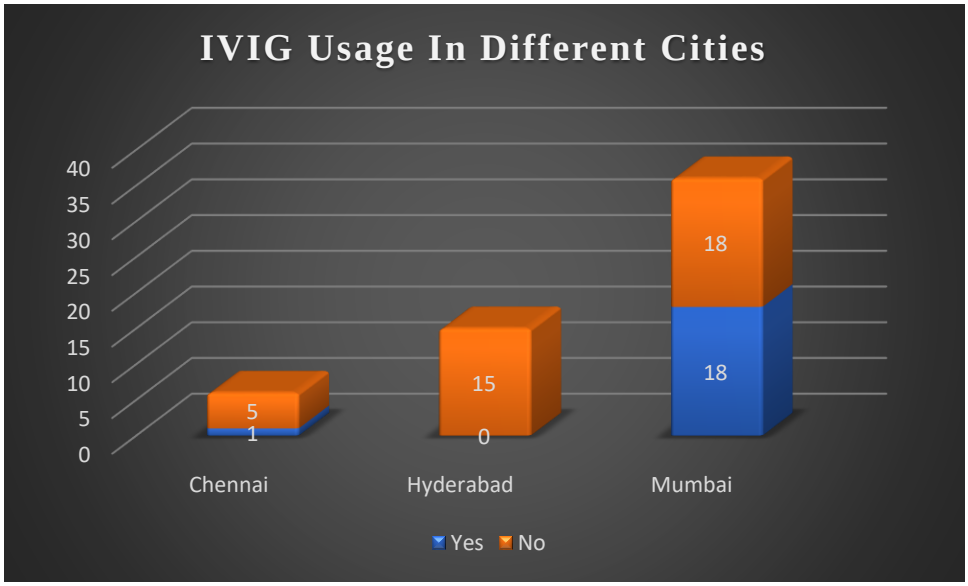
Interpretation- According to the graph majority of respondents did not responded to the supportive therapy provided by them. But those who were responding were bended towards the usage of Antibiotic, Antiviral and Antibiotic and Antiviral.



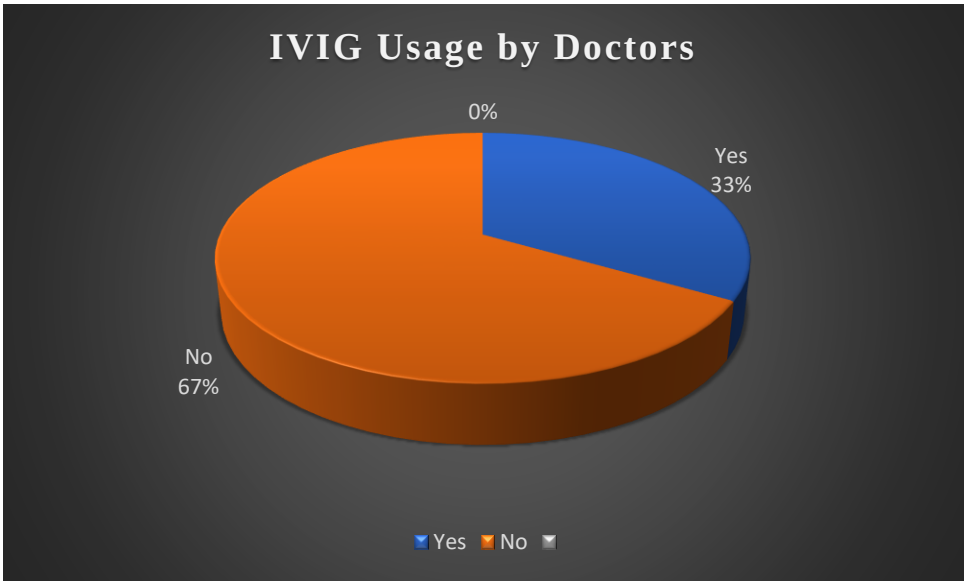
Interpretation- According to the graph various medical oncologist from all three cities uses antibiotic at most as compared antiviral, antiviral and antibiotic.



Interpretation- According to the above graph it's been found that haematologist incorporate antibiotic, antiviral, antibiotic and antiviral in the same proportion from all three cities.

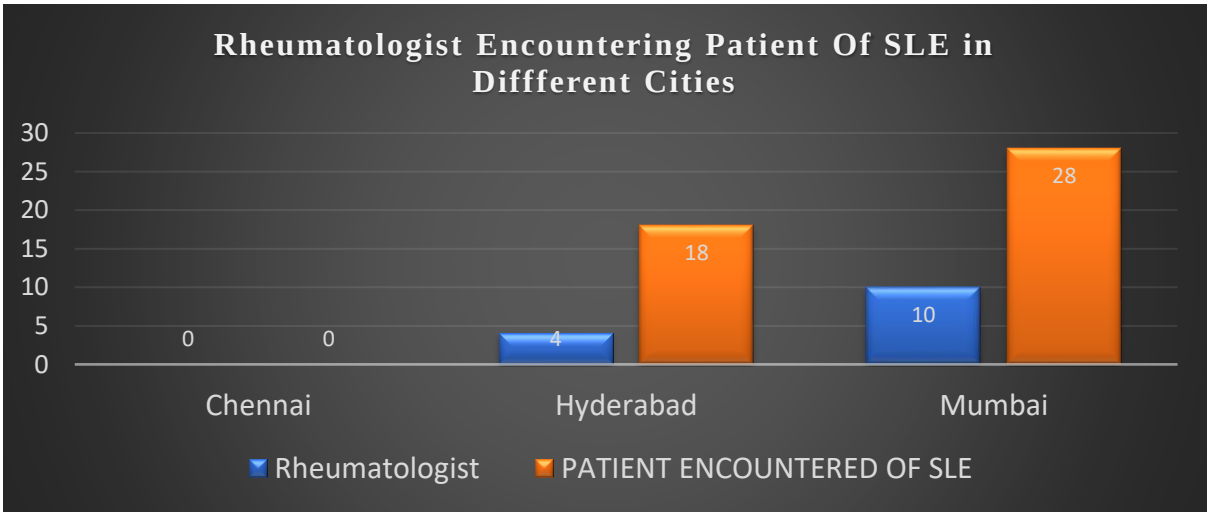


Interpretation- According to above graph IVIG is used maximum in Mumbai as compared to Hyderabad and Chennai.

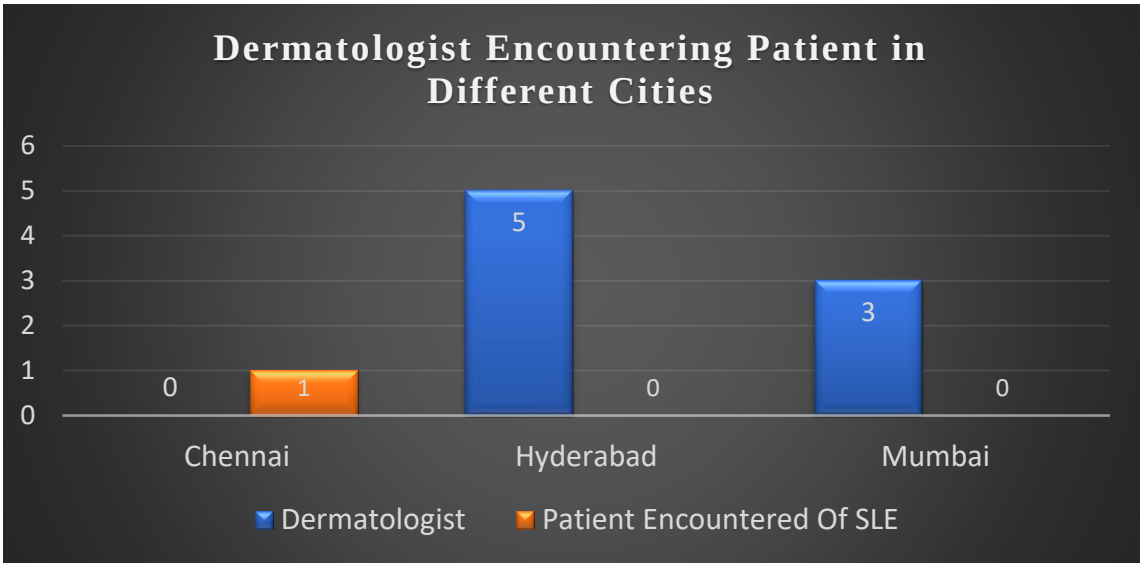


Interpretation- IVIG usage according to above pie chart is only 33% collected from all three cities and rest 67% do not use IVIG.

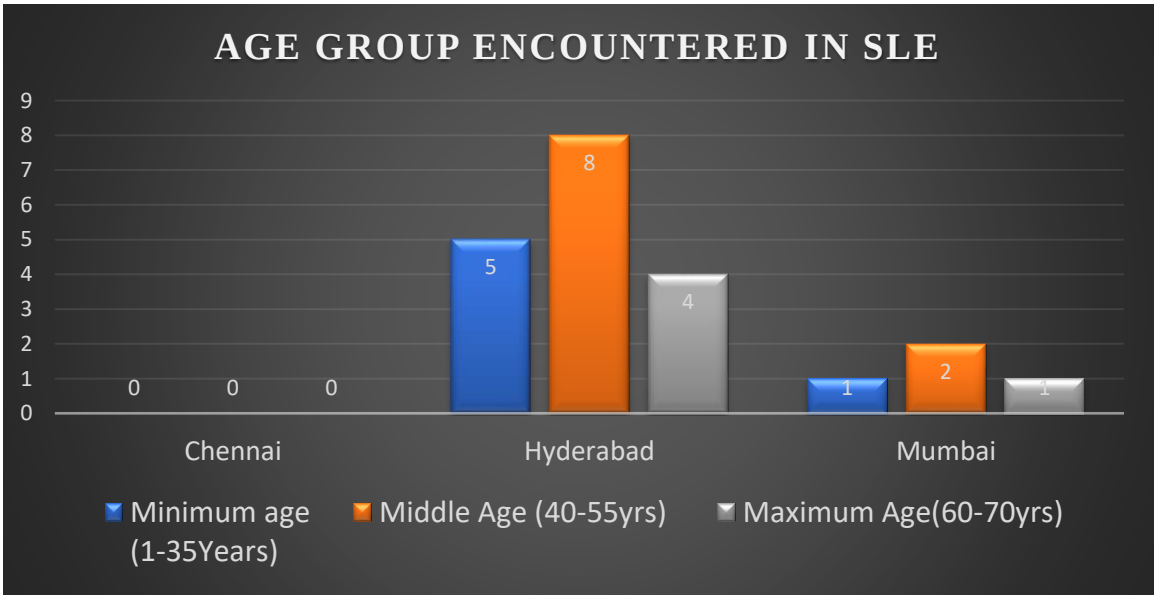
DATA ANALYSIS FOR SLE AND ANCA VASCULITIS:



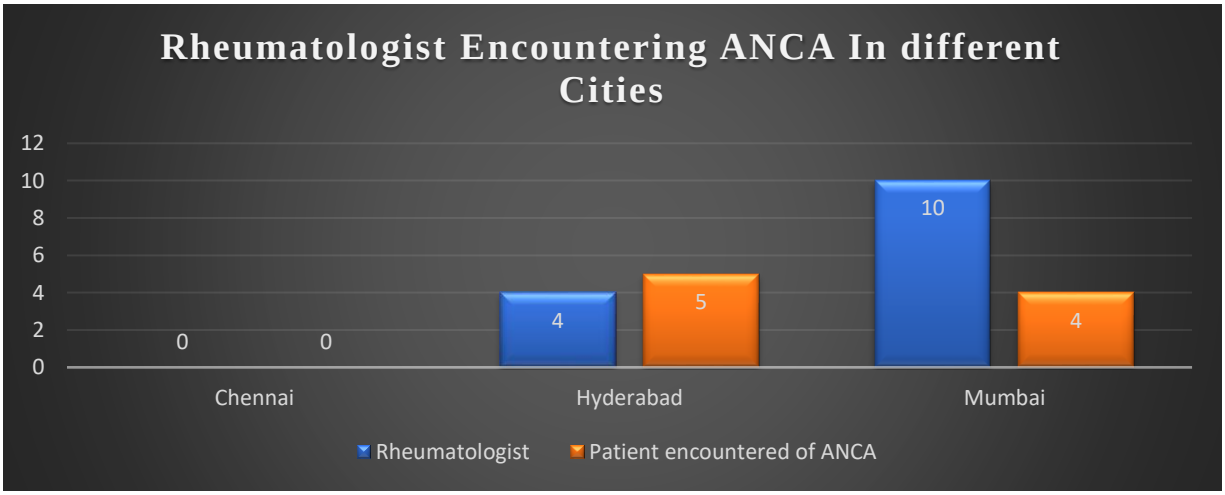
Interpretation- According to above graph rheumatologist encountering patient of SLE is highest in Mumbai as compared to Hyderabad and Chennai. In Hyderabad also rheumatologist encounter SLE.



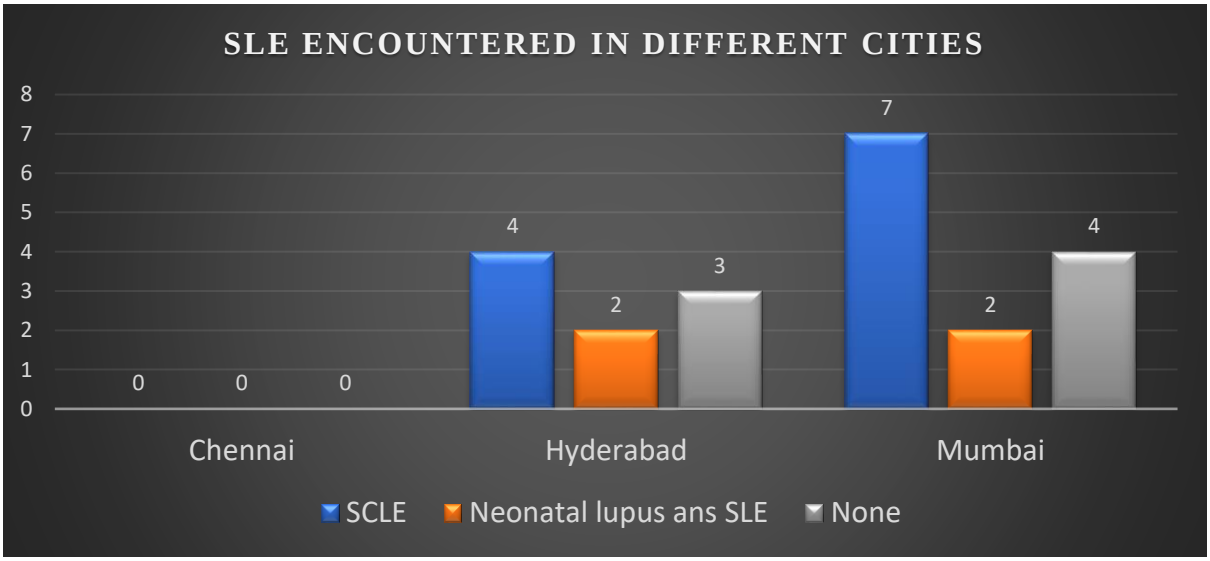
Interpretation- According to graph majority of dermatologist interacted in Hyderabad and Mumbai but none of them encountered SLE where as in Chennai SLE patient is encountered.



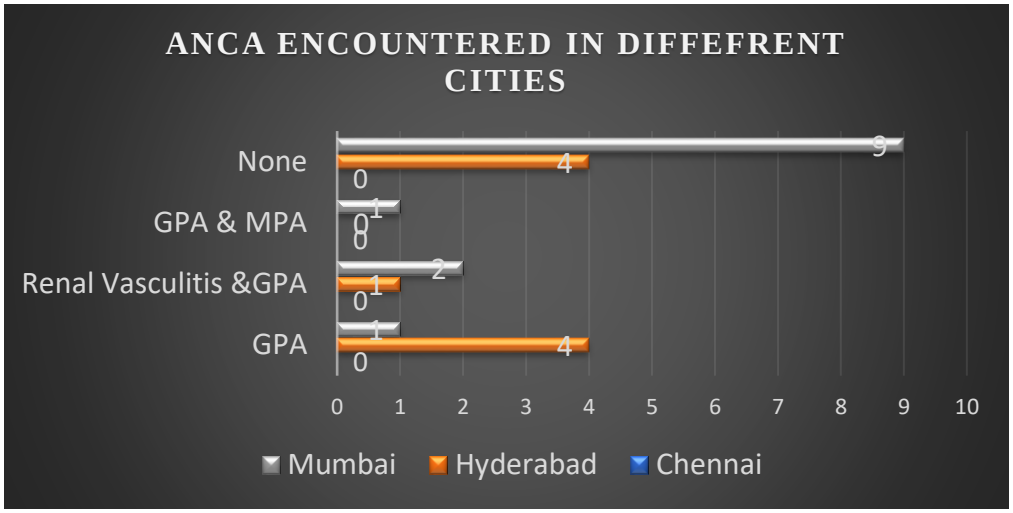
Interpretation- According to the graph it is found that Middle age patient has been encountered the most in Hyderabad and Mumbai.



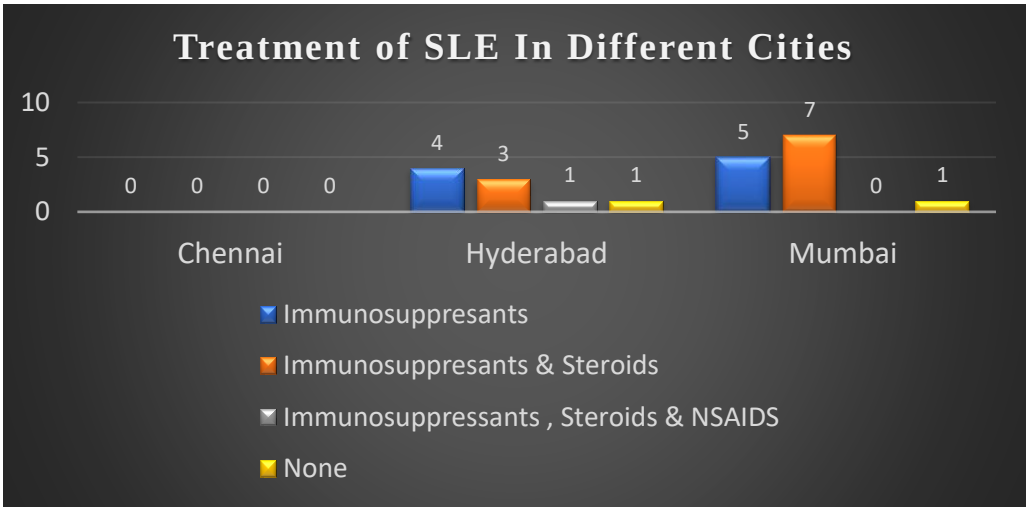
Interpretation- According to the graph majority of rheumatologist encountered was in Mumbai but ANCA Vasculitis is encountered most in Hyderabad .



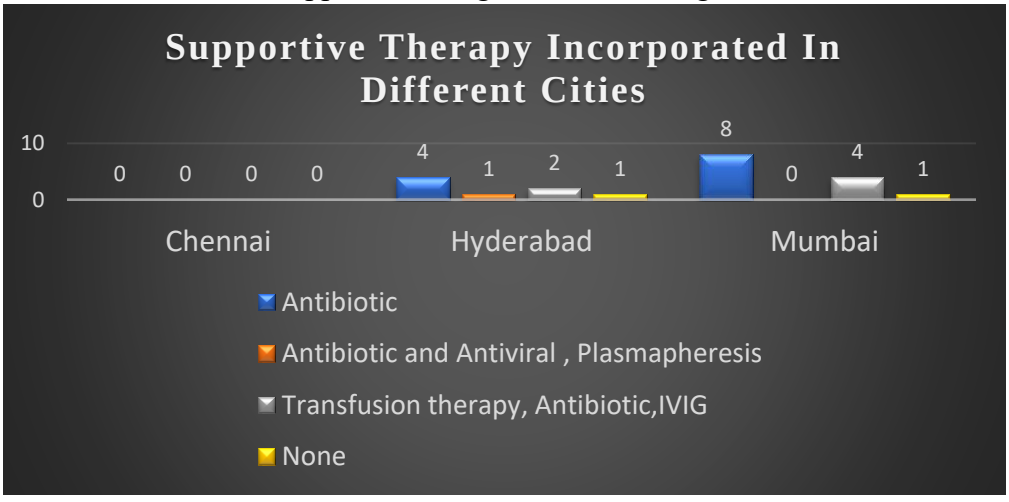
Interpretation- SCLE is the type of SLE which is encountered the most in Mumbai and Hyderabad. Neonatal is also found which is sometimes considered to be fatal.



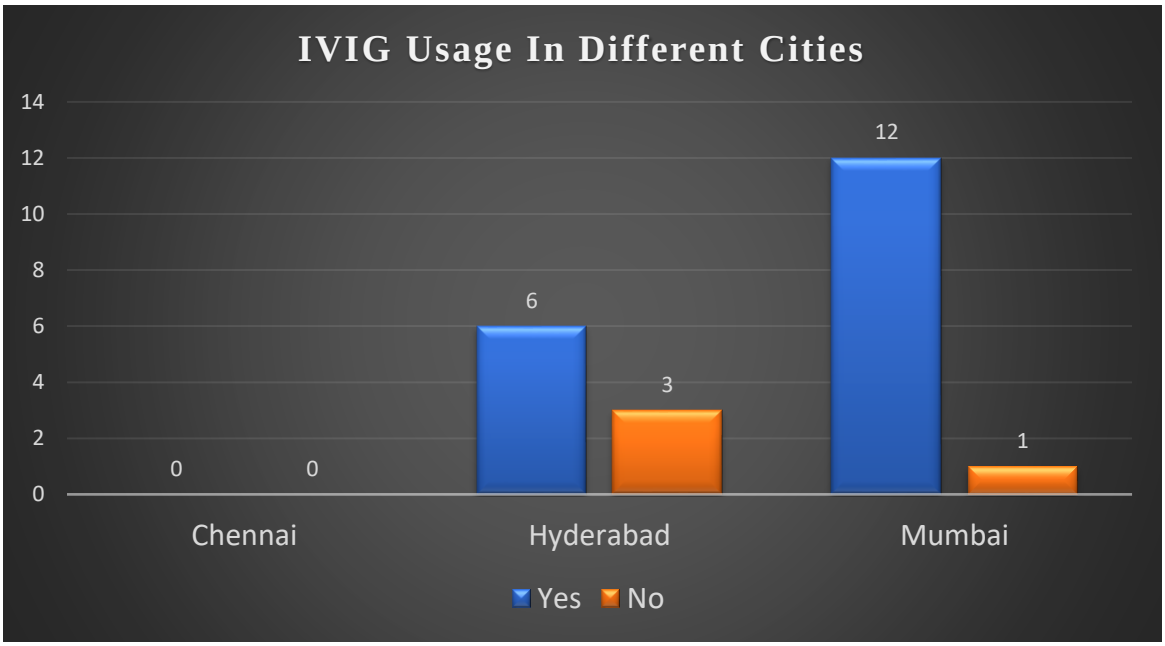
Interpretation- According to graph GPA is encountered in Hyderabad, as the rheumatologist do not encounter other types of ANCA they was unable tom provide the data.



Interpretation- According to graph the mostly incorporated treatment is Immunosuppresants and steroids, Immunosuppressants is given but it's usage is less.



Interpretation- According to above graph majority of supportive therapy is incorporated in Mumbai which is considered to be Antibiotic. In many of the hospital doctors too incorporate transfusion therapy with antibiotic and IVIG.



Interpretation- IVIG usage pattern is highest in Mumbai and Hyderabad, as the rheumatologist are aware about the standard regimen and safety and efficacy of IVIG.

LIMITATIONS:

- As the project deals with the rare disorder segment thus to interact with super speciality division was quite difficult task as they are overcrowded by the cancer patient.
- To keep probing attitude with full of perseverance becomes challenging.
- Doing survey on the name of student becomes very challenging as the frequently asked question is what benefit would you provide if data is being provided.
- Handling the random question of doctors dealing with rare disorder is quite challenging.

CONCLUSION:

According to various research article IVIG should be used in autoimmune disorder and various blood related problems as IVIG is responsible to boost up the immune system .But the present scenario of IVIG is totally different as in the survey for CLL and Multiple Myeloma , SLE and ANCA Vasculitis doctors are not much interested to go for IVIG as supportive therapy. As according to them IVIG is not having standard regimen and many people are not able to afford it. During the entire period of project and specially to make interaction possible with medical oncologist, hematologist and surgery division is challenging one as the doctors are surrounded by patient thus, we should try make our identity meaningful with the justified point. There also lies a misconception regarding the usage of IVIG which was quite surprising. According to study it was found that in Mumbai doctors are well aware about IVIG and also incorporating it in treatment as a supportive therapy. Affordability criteria has been mentioning since the starting interaction as well, so basic problem in this arena is the fractionation or componentization as this play very important role and also sterility should be maintained. Thus, at last it was found that few parts like awareness, affordability, must be given attention.

RECOMMENDATION:

- Enriching Doctors knowledge regarding IVIG is very important.
- Awareness in not only one region but each and every region of country is required as Doctors are having misconception regarding standard regimen.
- Affordability factor should also be noticed by building few componentization unit.
- According to the pilot study that has been accomplished, its recommended that reason behind the less usage of IVIG is its awareness and misconception of the standard regimen, thus awareness must be created in Chennai and Hyderabad . Also Affordability is one criteria due to which oncologists do not go for this supportive therapy. To make it affordable one suggestion was the increment of the componentization unit.

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Annexure 1.

INDIAN INSTITUTE OF HEALTH MANAGEMENT RESEARCH

Jaipur , Rajasthan

IIHMR UNIVERSITY

QUESTIONNAIRE

PREFERRED TREATMENT OPTIONS IN ONCOLOGY

(CHRONIC LYMPHOCYTIC LEUKAEMIA AND MULTIPLE MYELOMA)

Name _____ **Speciality** _____

Hospital _____

Email ID _____

1. Frequency of Case of Chronic Lymphocytic Leukaemia and Multiple Myeloma?

CHRONIC LYMPHOCYTIC LEUKAEMIA	**MULTIPLE MYELOMA**
1.Twice in Week	1.Twice in Week
2.Thrice in Week	2.Thrice in Week
3.Any other	3.Any other

2.Any cases reported apart from Regular Age Group?

CHRONIC LYMPHOCYTIC LEUKAEMIA	**MULTIPLE MYELOMA**

3.Which Line Of Treatment do you incorporate the most for chronic lymphocytic leukaemia and multiple myeloma?

- Chemotherapy
- Targeted Therapy
- Radiation Therapy
- Monoclonal Antibodies
- Any other

Why_____

5.Do you incorporate any supportive therapy with the preferred line of treatment?

- Yes
- No

Why _____

6.Do you use IVIG as supportive Therapy?

- Yes
- No

Why _____

7.Dosage pattern OF IVIG preferred in chronic lymphocytic leukaemia and Multiple Myeloma?

CHRONIC LYMPHOCYTIC LEUKAEMIA	MULTIPLE MYELOMA
(a).1 in every month(0.4gm/kg)	(a)1 in every month(0.4gm/kg)
(b).1 in 15 days (0.4gm/kg)	(b)1 in 15 days (0.4gm/kg)
(c).1 in two months(0.4gm/kg)	(c)1 in two months.(0.4gm/kg)
(d).Any Other	(d)Any Other

ou

9.Which of the following attributes influence you to incorporate IVIG as supportive therapy?

- Efficacy
- Affordability
- Accessibility
- Safety

Annexure .2.

INDIAN INSTITUTE OF HEALTH MANAGEMENT RESEARCH

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QUESTIONNAIRE

Preferred Treatment Options in Rheumatology

(Systemic Lupus Erythematosus and ANCA Vasculitis)

Name _____ **Speciality** _____

Hospital _____

Email ID _____

1.Frequency of Case of Systemic Lupus Erythematosus and ANCA Vasculitis?

Systemic Lupus Erythematosus	ANCA VASCULITIS
1.Three in Week	1.Twice in Week
2.Five in Week	2.Thrice in Week
3.Any other	3.Any other

2.Which age group is more prone to Systemic Lupus Erythematosus and ANCA Vasculitis?

SYSTEMIC LUPUS ERYTHEMATOSUS	ANCA VASCULITIS
(a)0-15(Years)	(a)0-15(Years)
(b)15-35(Years)	(b)15-35(Years)
(c)35-45(Years)	(c)35-45(Years)
(d)45 and More	(d)45 and More(Years)

3.Which Systemic Lupus Erythematosus is most common among patients?

- Discoid lupus erythematosus
- Neonatal lupus
- Subacute cutaneous lupus erythematosus

4.Which type of ANCA Vasculitis is encountered the most among patients?

- Renal limited vasculitis
- Microscopic polyangiitis (MPA)
- Granulomatosis with polyangiitis (GPA)
- Eosinophilic granulomatosis with polyangiitis (EGPA)

5.Choice of Main Treatment for Systemic Lupus Erythematosus?

- Immunosuppressive medications
- NSAIDs
- Corticosteroids
- Any other

Why_____

6.Choice of Main Treatment for ANCA Vasculitis?

- Glucocorticoids
- Cyclophosphamide
- Immunosuppressants
- Any other

Why._____

7.Do you incorporate any supportive therapy with the preferred line of treatment?

- Yes
- No

Why _____

8.Do you use IVIG as supportive Therapy?

- Yes
- No

Why _____

9.Dosage pattern of IVIG preferred in Systemic Lupus Erythematosus and ANCA Vasculitis?

Systemic Lupus Erythematosus	ANCA Vasculitis
(a).1 in every month	(a).1 in every month
(b).1 in 15 days	(b).1 in 15 days
(c).1 in two months.	(c).1 in two months.
(d).Any	(d).Any Other

11.Which of the following attributes influence you to incorporate IVIG as supportive therapy?

- Efficacy
- Affordability
- Accessibility
- Safety