Summer Training at

PlasmaGen Biosciences
(April-June 2013)

Study on Hyper Immune Plasma Proteins in Tier 1 and Tier 2 cities

By
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Under the guidance of
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Post Graduate Diploma in Pharmaceutical Management
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2013

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Certificate

This is to certify that HIMANSHU RAO student of Post Graduate Diploma in Pharmaceutical management (PGDPM) from Institute of Health Management Research, Jaipur Batch 4th, has successfully undergone his summer training at PlasmaGen Biosciences, Bangalore and has done project on:

- 'Study on Hyper immune plasma proteins in Tier 1 and Tier 2 cities'

The candidate has successfully carried out the mentioned studies assigned during his summer training from 25 April 2013 – 15 June 2013 and his approach towards study was sincere, scientific and analytical.

We wish him success in all his future endeavours.

Dr. Ashok Kaushik

Dean acedmics and student affairs

IHMR, Jaipur

8/7/14

Mr. Abhishek dadhich

Assistant professor

IHMR, Jaipur

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ORGANISATION PROFILE OF PLASMAGEN BIOSCIENCES

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.

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.

Values:

LEADERSHIP
Courage & Passion
RESPECT & INTEGRITY
Transparent Work Environment
QUALITY

Reflection of our Excellence

SOCIAL RESPONSIBILITY

People & Environment

HARMONY

Work-life Balance

CUSTOMER SATISFACTION

Exceed Expectations

Specialties

Plasma Protein Therapy, Plasma Products, ImmunoGlobulins, Plasma Molecule Specialist

PROBLEM STATEMENT:

GAP analysis - demand and supply of Hyperimmune proteins in the Indian plasma product industry.

TITLE:

"Hyper-immune Plasma Proteins in Indian Tier I and Tier II Cities- determine the public health perspective on the availability, affordability, safety, consumption pattern and market potential of each product."

Objectives:

For each category of product:

- To estimate awareness about hyperimmune products
- To understand public health perspective of hyper immune products in the regions.
- To determine the number of diagnosed cases in the given region.
- To understand the disease management by doctors
- To analyze whether the existing demand for the products are fulfilled.
- Perception of doctors in these regions regarding the hyper immunes.

- Factors affecting the growth of hyperimmune plasma protein market in Tier I and Tier II cities

To determine the factors that would promote usage of these products in Tier I and Tier II cities

BACKGROUND OF STUDY:

Introduction to plasma industry:

Whole blood consists of two main components; red blood cells which represent about 45% of the volume of a unit of blood, and plasma, which is the liquid portion of blood, making up the remaining 55%. Plasma can be separated from whole blood by a procedure called "plasmapheresis" in which whole blood is drawn from a donor's vein into a machine which separates plasma from the red cells by filtration or centrifugation. Once the red cells are separated from the plasma, they are returned to the donor using the same vein or a different one, depending on the machine used. The human body regenerates plasma within a few days, unlike red blood cells which need a few weeks. For this reason, a donor can donate plasma more frequently – up to twice a week in the United States – than whole blood.

Red cells, and whole blood, are used to treat traumatic or surgical blood loss, as well as anemia. Plasma is indicated in a number of indications, in particular deficiencies of certain coagulation factors, as well as trauma, schock and many other medical condictions. Plasma serves also as the raw material to manufacture a number of "plasma-derived" drugs through an industrial process called "fractionation" which isolates each "fraction" of the plasma and turns them into life-saving drugs: coagulation factor concentrates, immunoglobulins, albumin and many others.

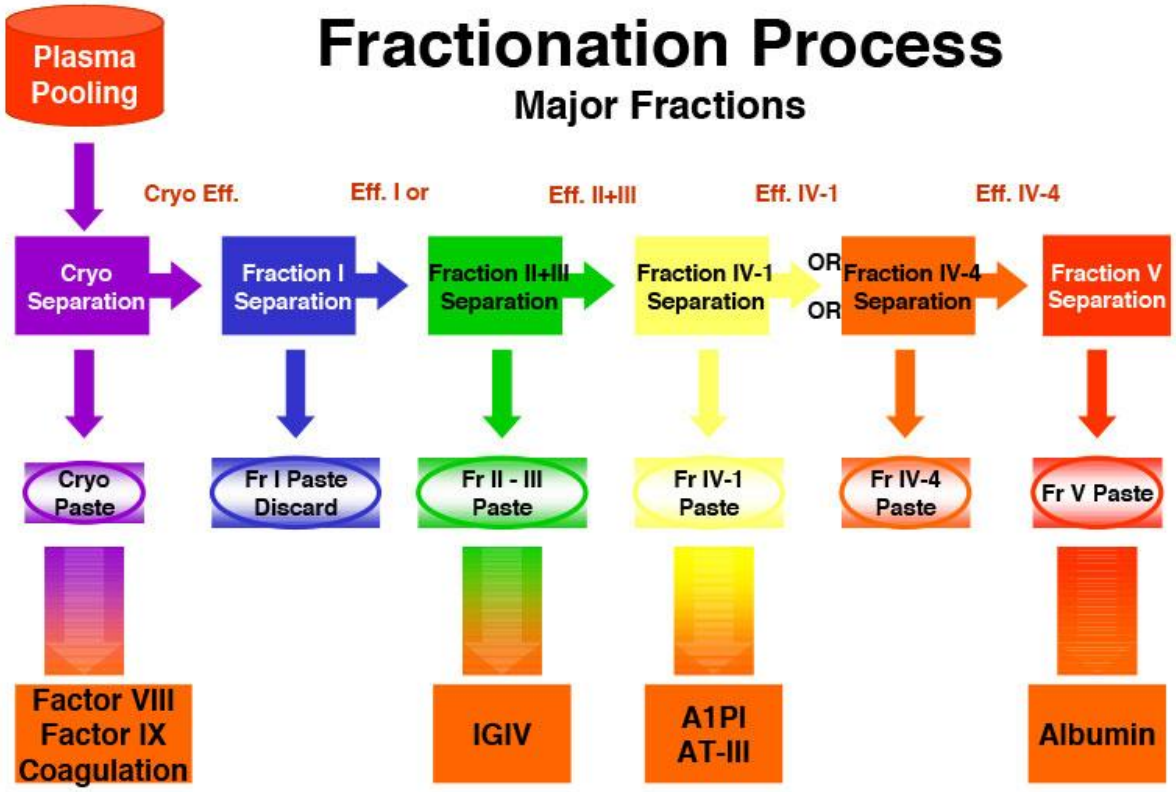
history of blood fractionation:

The history of plasma fractionation began with the need to develop blood serum products to help soldiers suffering from shock and burns in the Second World War. Dr. Edwin Cohn, of Harvard University, was a key figure involved in the development of a process to separate proteins from

human plasma, and the “Cohn fractionation process” which still forms the basis of most modern plasma fractionation facilities bears his name.

Originally, the aim was to separate albumin, which represents 55-60% of the total protein volume in plasma for use in injured soldiers, but over time, additional proteins were separated and used clinically. The Cohn fractionation process originally developed in the 1940’s involves modifying the pH, ethanol concentration and temperature to separate proteins through precipitates into five “fractions” (I-V). The first fraction is “cryoprecipitate” which contains “factor VIII,” “factor IX” and other heavy proteins, the first two of which are used in hemophilia treatment.

Originally, hemophilia patients had to use cryoprecipitate to control bleeding, but in the 1960’s, methods were developed to purify factor VIII and later factor IX from fraction I, and hemophilia patients were able to use these purified products for treatment over time. In the 1950’s intramuscular immunoglobulin (IMIG) was developed from fractions II and III and introduced as replacement therapy for patients with congenital antibody deficiencies. The intramuscular injections were painful only small volumes could be administered, which did not allow for an adequate dosing. In the 1980’s, purification methods had improved enough to enable the production of “intact” molecules with full biological efficacy, allowing the development of the first commercial preparations of intravenous immunoglobulin (IVIG)



Clinical use of plasma products:

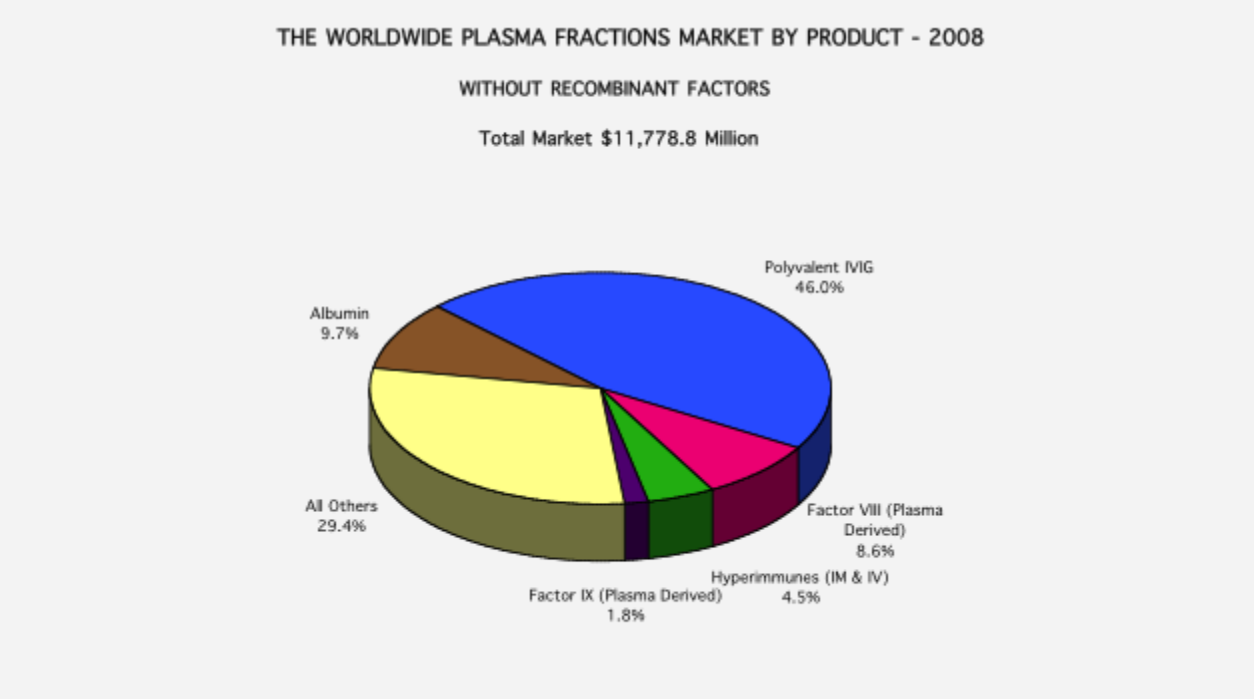
Immune globulins (IgG): they are produced by B-cells in the body to identify and aid in the destruction of foreign molecules including bacteria and viruses. They are the main function of the body's humoral immune system. Replacement therapy with immune globulins has been used extensively since their commercial introduction in the 1950s. Two categories of immunoglobulin preparations exist today:

Intravenous and subcutaneous immunoglobulins (IVIG/SCIG) are the most common preparations, and are prescribed as a replacement therapy for congenital antibody deficiencies. In recent years, they have been found to be increasingly efficacious in treating neurological conditions, as well as diseases in other areas, including hematology, infectious diseases, etc. Over 200 indications have been identified for IVIG/SCIG.

a. **Hyperimmune immunoglobulins** are preparations in which the level of some specific antibodies has been enriched to target a particular antigen, as opposed to the naturally diverse set of antibodies present in IVIG and SCIG. Specific hyperimmune preparations are made for specific conditions, including; Anti-D (anti-RhoD), Cytomegalovirus (CMV), Hepatitis A and B, Rabies, Tetanus, and Varicella.

Plasma economics:

Even though many proteins may be separated from plasma and commercialized, some of them are in more demand than others. Those generating the strongest demand determine the volume of plasma needed for fractionation. By maximizing the volume of plasma fractionated to make each product in adequate quantity, a company can maximize its revenues and profitability.



Source: the Marketing Research Bureau, Inc. The Worldwide Plasma Proteins Market 2008

In the past twenty years, intravenous immune globulin (IVIG) has clearly been in higher demand than any other plasma product. Therefore, its demand has determined the volume of plasma needed on a global scale. As such, it has become the driver of the plasma market, displacing

factor VIII, which was the market driver until the early 1990s, when “recombinant factor VIII came out on the market. Today, IVIG accounts for 40-50% of the global plasma proteins market (approximately $14 billion) although this percentage varies significantly by region. Albumin and plasma-derived factor VIII (pdFVIII) each have a smaller share of the market (10-15% each) again with wide regional variations. Both products are generally fractionated from plasma along with IVIG while others, such as factor IX, alpha-1 antitrypsin or antithrombin III are not produced from every liter of plasma.

Plasma procurement

Plasma Collection:

To obtain enough raw materials for the production of plasma products, millions of liters of plasma are needed annually. Some of the plasma is obtained by separating plasma from red blood cells after whole blood donation, for example at a Red Cross Blood Drive. This plasma is called “recovered plasma” because the goal of the blood collection organization it to obtain red cells and platelets, and plasma is a by-product. Another type of plasma for fractionation, called “source plasma,” is generated by dedicated plasma collection centers which collect plasma from donors through plasmapheresis machines (these machines extract only the plasma from the donor, and not the red cells). Plasma donors are compensated for their time to donate while whole blood donors are not.

It is essential for each company to have access to a sufficient quantity of plasma to meet its production objectives, as it is the raw material to manufacture all the therapeutic proteins.

To this end, the large, multinational plasma companies, the “fractionators” now own most of the plasma collection centers in the U.S. where they collect most of the plasma they need. Source plasma is also produced in significant quantities in China, Germany, Austria and the Czech Republic.

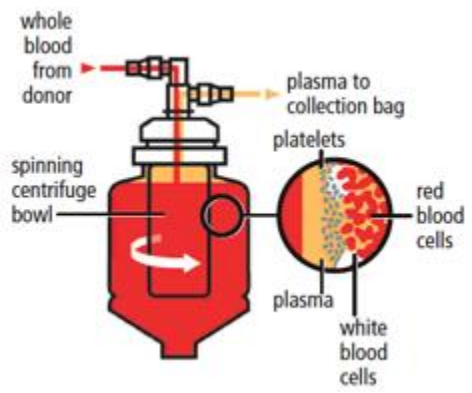


Diagram of automated plasma collection procedure

Source: CSL Behring

Effective Use of a Finite Supply:

Plasma-based products can only be produced from plasma, and plasma can only be extracted from human donors. Consequently, plasma is a finite resource that cannot be replicated or mass produced in large industrial processes. Thus, the plasma must be used efficiently by producing as many products as possible from each liter collected. For example, it is better to produce IVIG, albumin and pdFVIII from a liter of plasma than just the first two products. Furthermore, efficiency is also achieved by improving the yield at which each product is extracted from the plasma, as well as finding new proteins with therapeutic potential in the plasma. Continuing efforts in all these areas are underway to improve the efficiency and profitability of plasma fractionation.

RESEARCH METHODOLOGY:

1) Data collection:

   Primary data: data collection source

   - questionnaire to doctors
   - interviews

   Secondary data:

   - newspapers
   - journals and magazines
   - internet

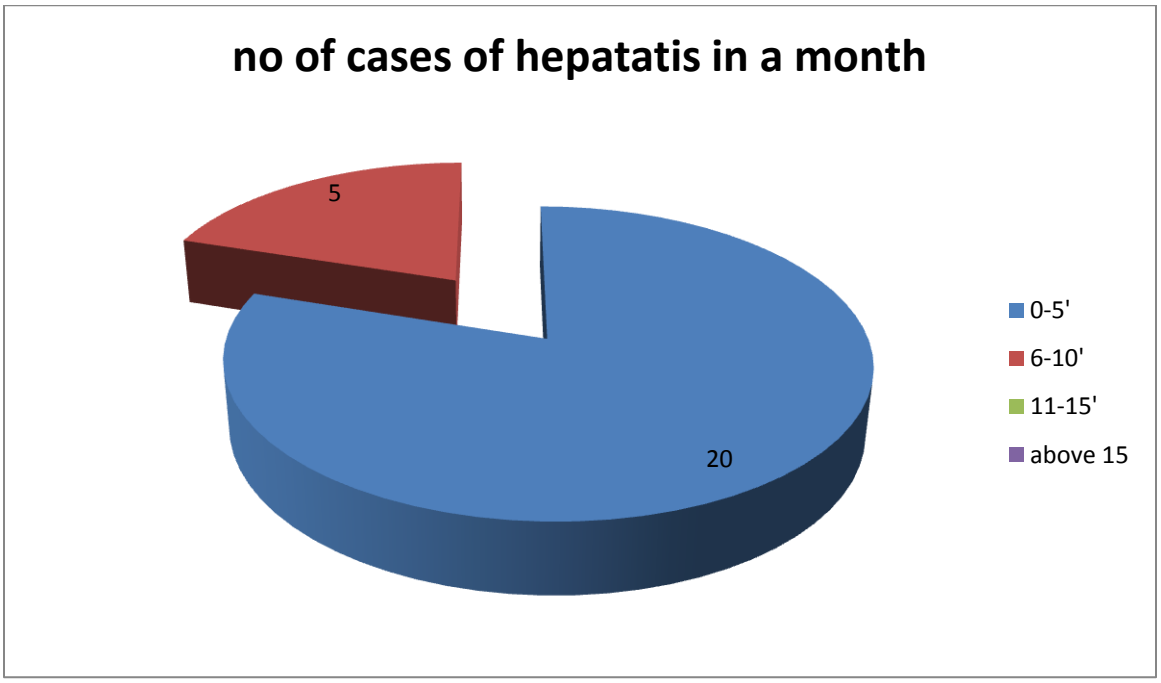
2) type of study design: the type of study design used for this research is cross sectional study design
3) research instrument:
    - questionnaires: structured and open ended questions
    - interviews: responded were interviewed on use of immunoglobulins

the study is predominantly based on primary data, however conceptual data is collected from journals,text books.

DATA ANALYSIS:

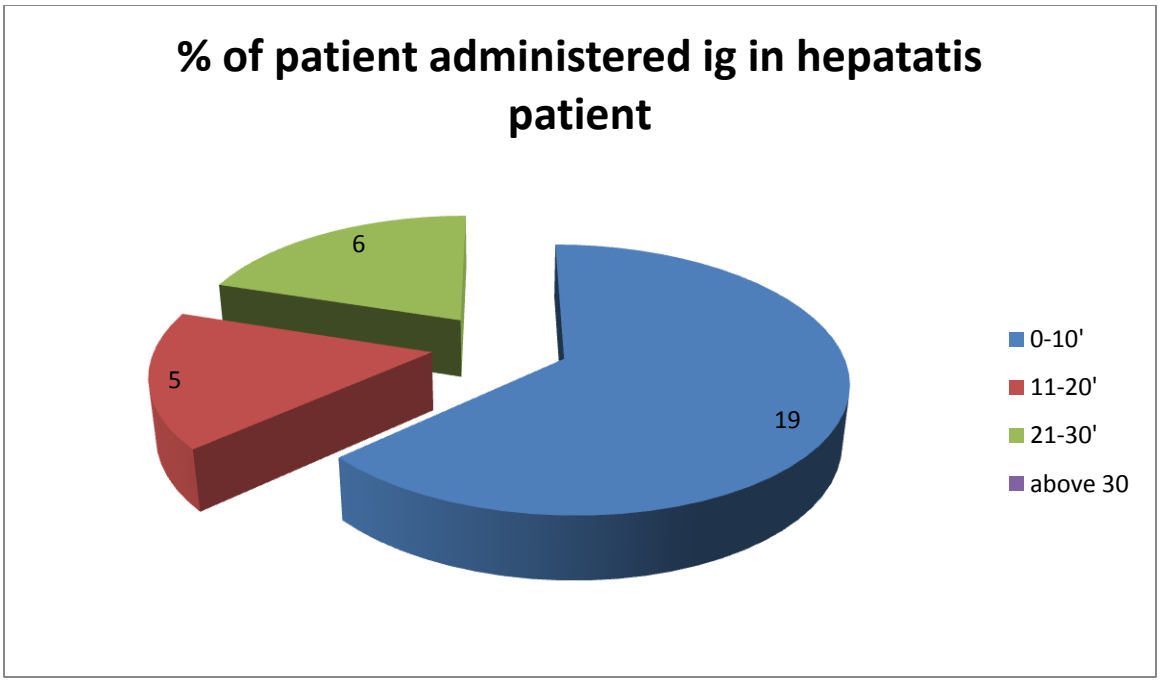
Analysis of hepatitis B:

A survey of 24 doctors is taken into consideration.

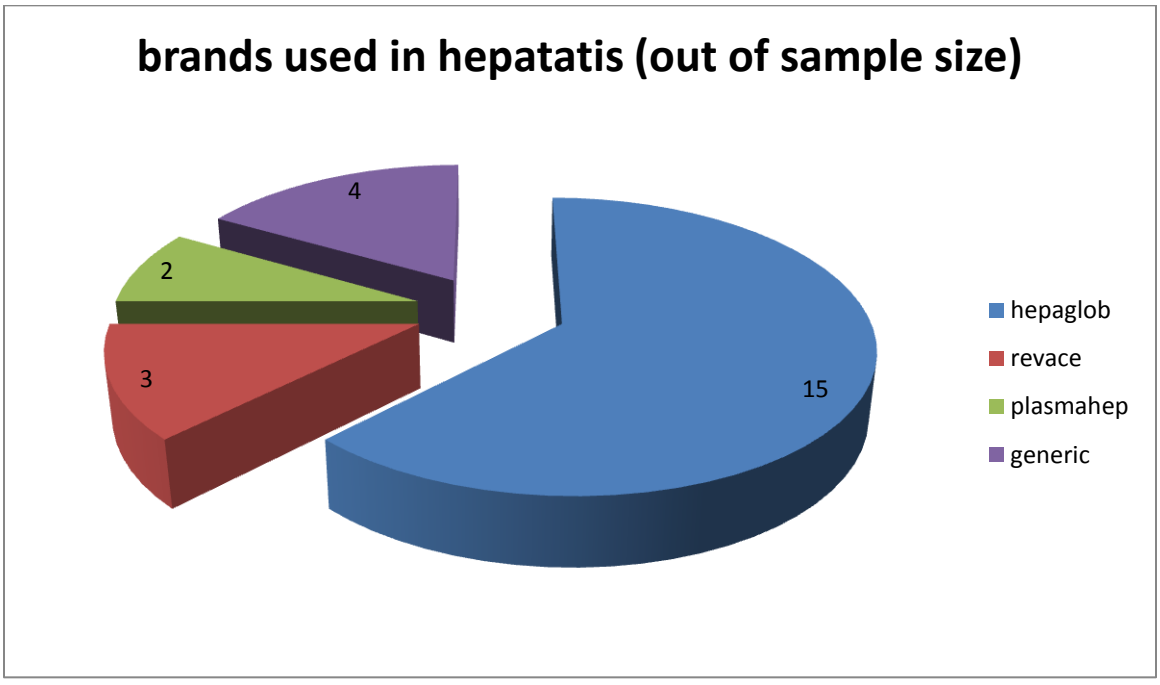


20 out of 24 doctors had less than 6 patients per month

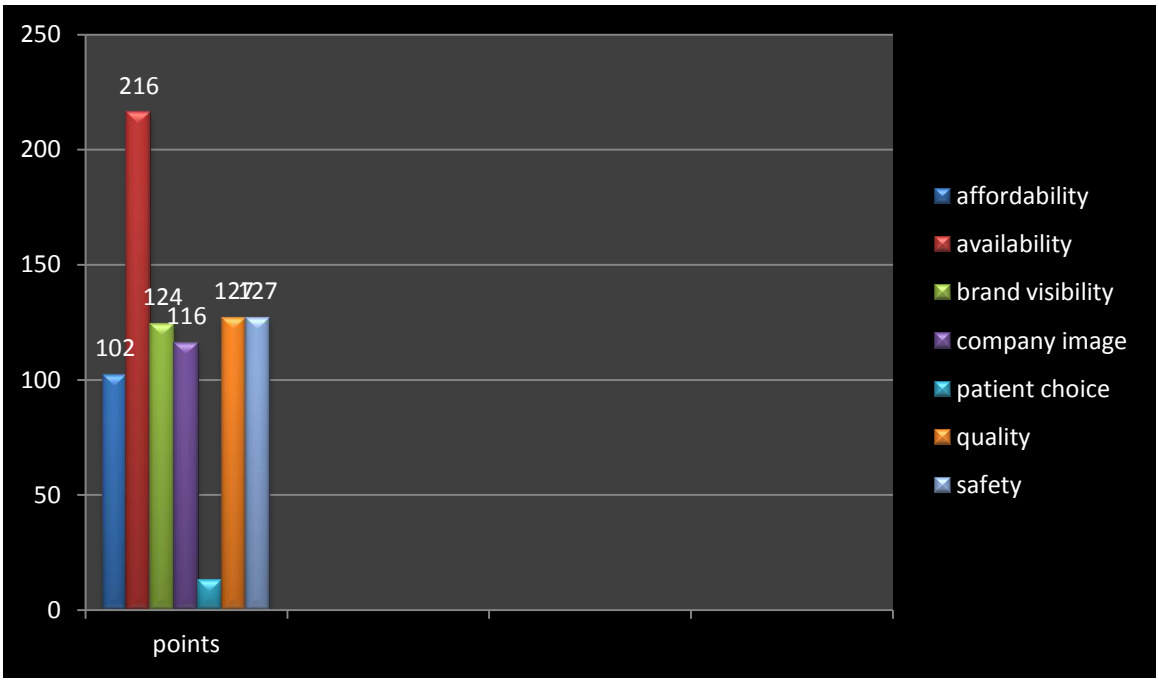
Only 5 out of 24 doctors said that they have 6-10 patients per month



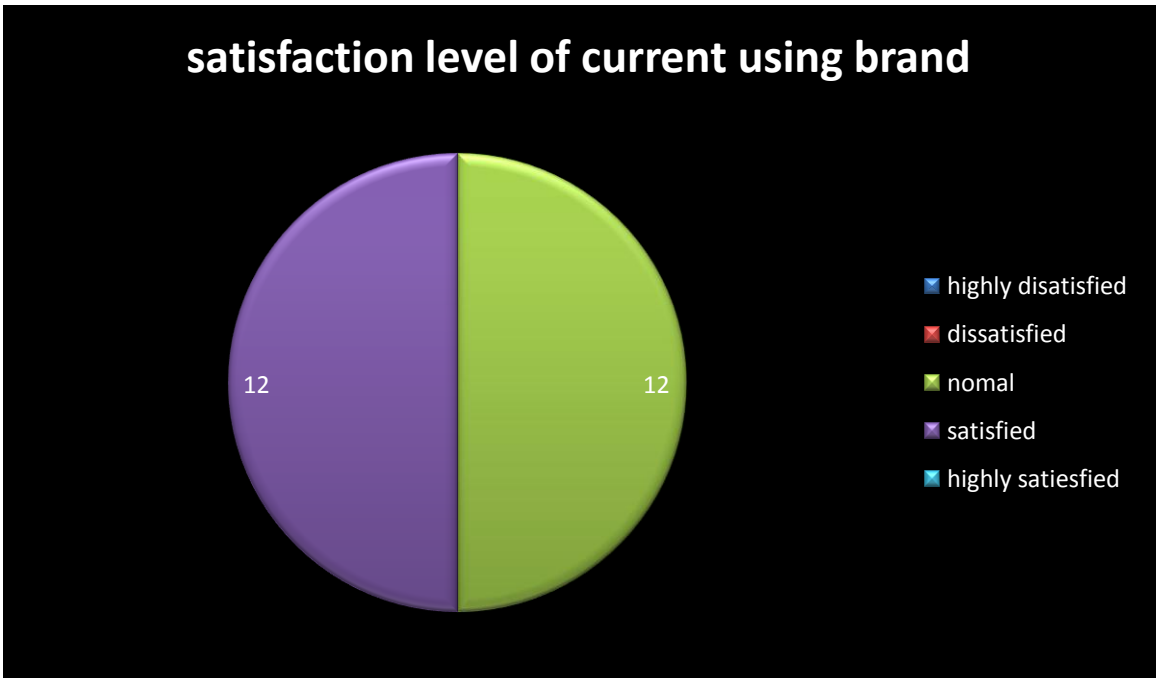
19 doctors administer immunoglobin above 30% of there patient pool of hepatitis



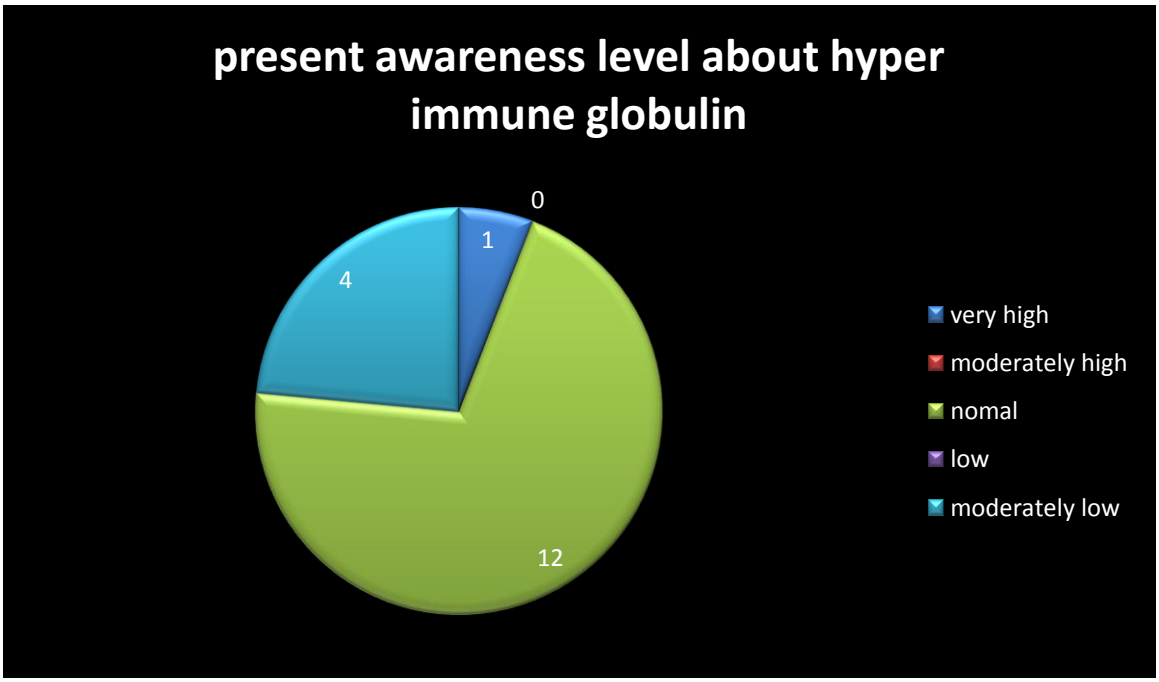
Hepaglob by 4 plasmahep by 2 and revace was used by 3 doctors out of 24



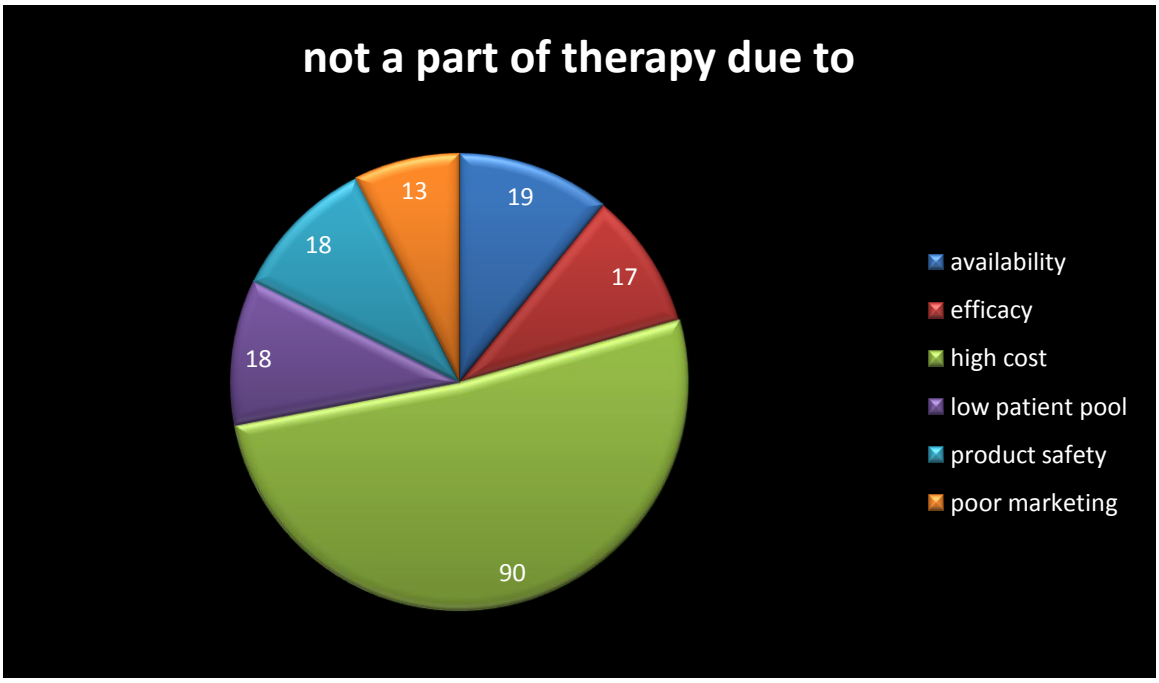
Choice of brand was due to availability brand visibility quality and safety



Out of 24 sample size 12 were normal and 12 were satisfied with the current brand

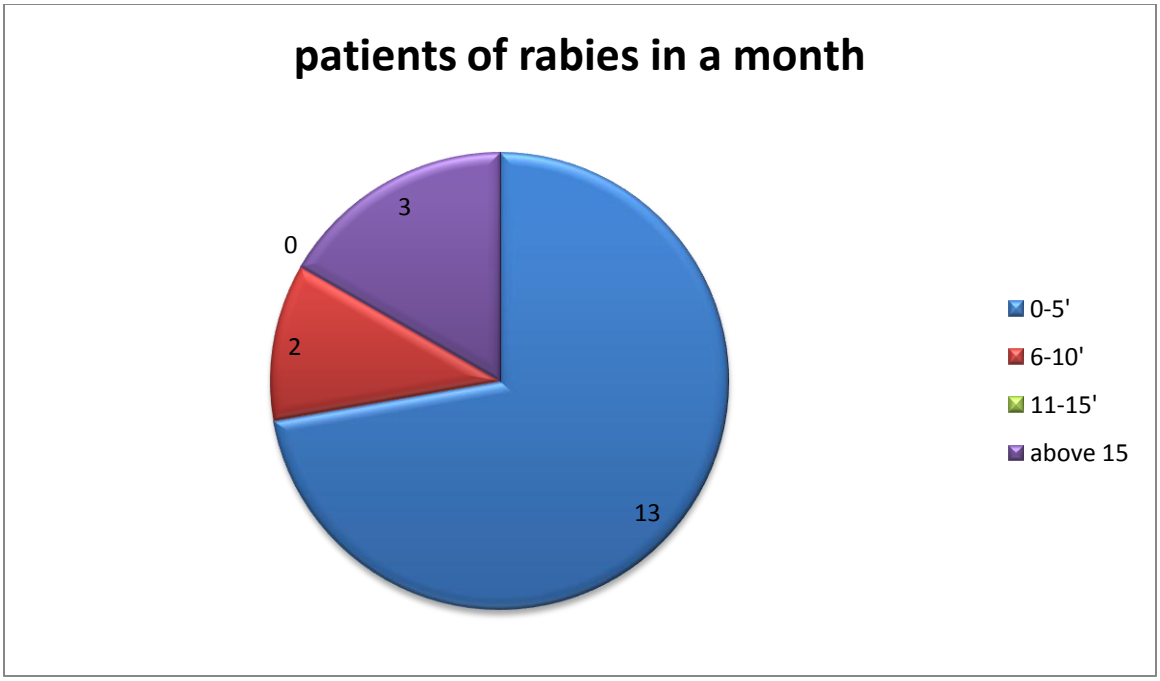


4 of the respondents said that awareness level was moderately low

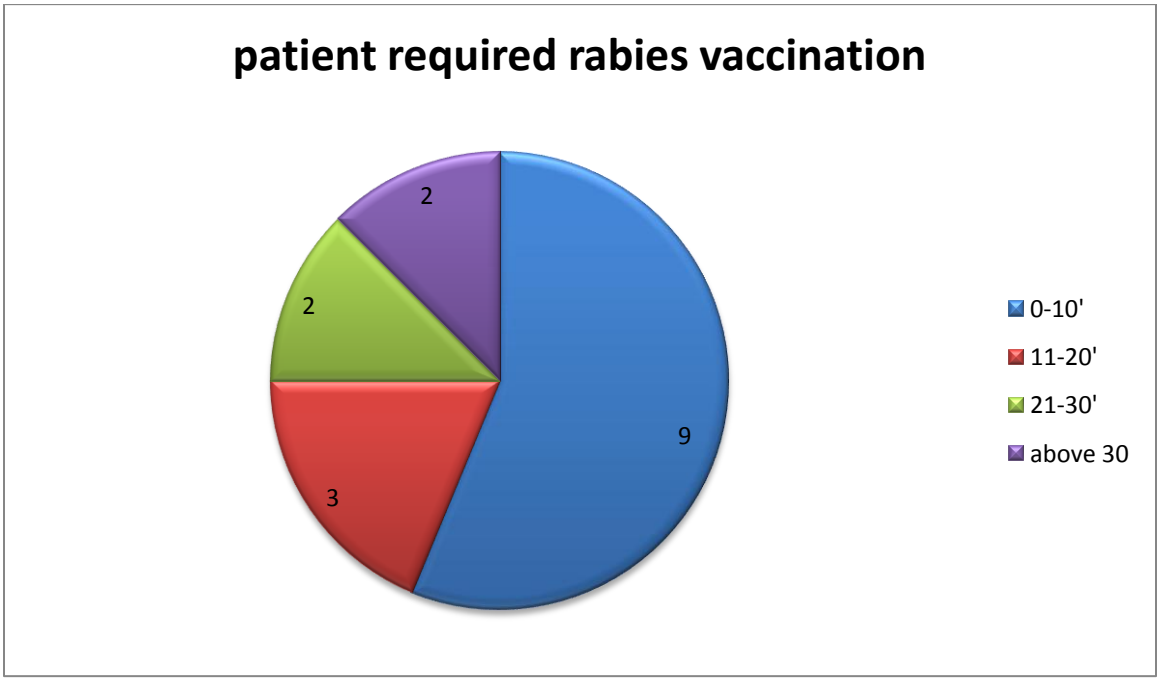


High cost of these immunoglobulins is a major issue which affect the prescripition of doctors

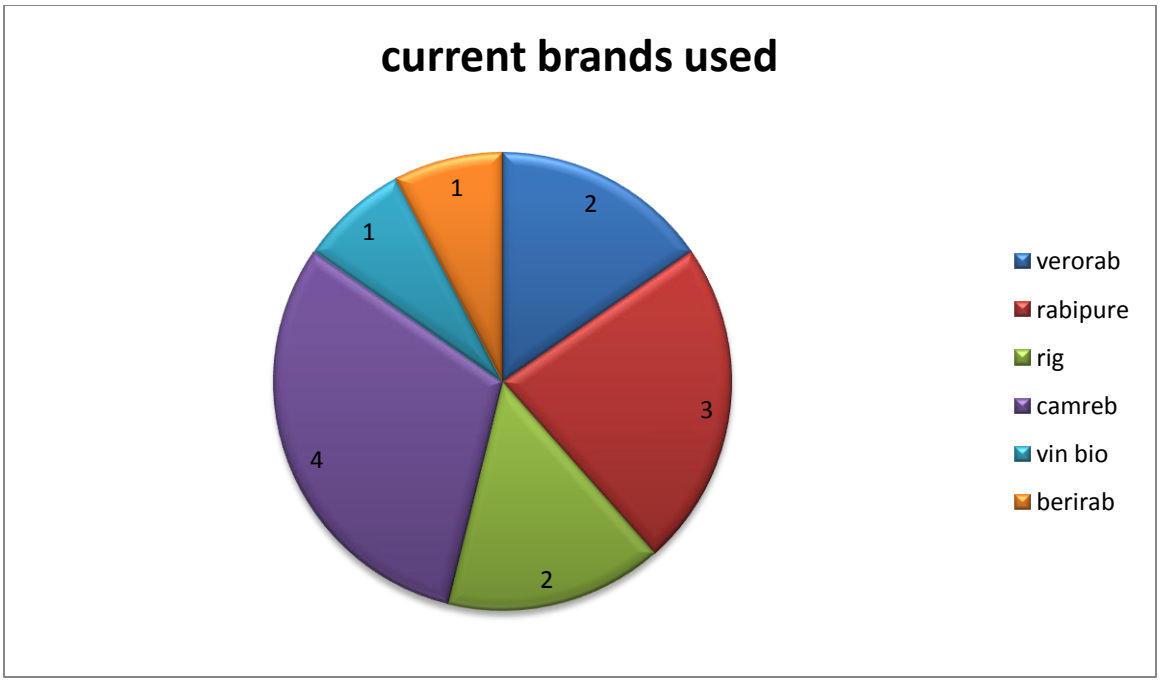
Analysis of rabies: 20 respondents



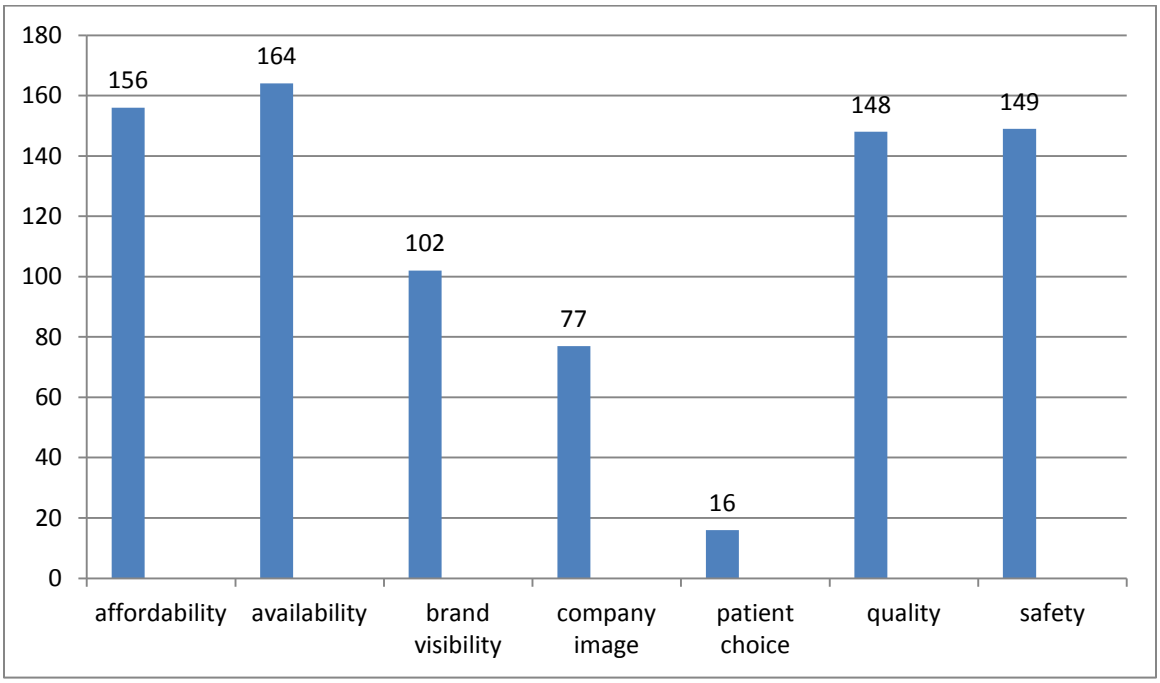
Out of 20, 13 doctors were having more than 15 patients of rabies per month



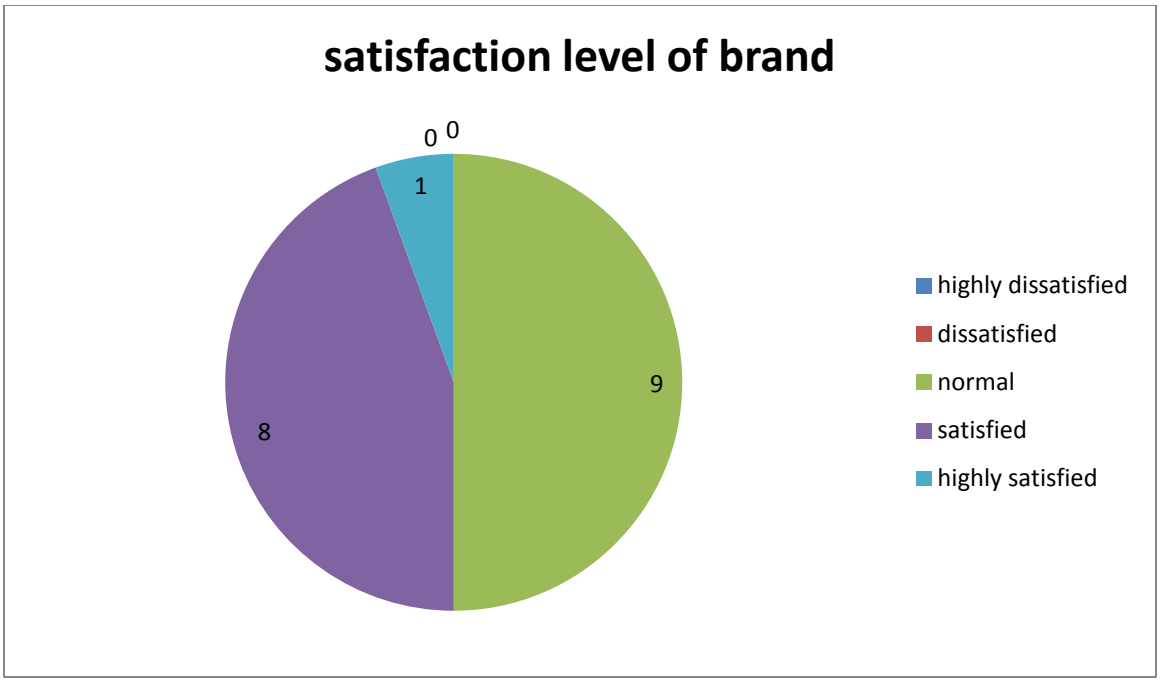
9 of the doctors used to give immunoglobulin in more than 30% of patients



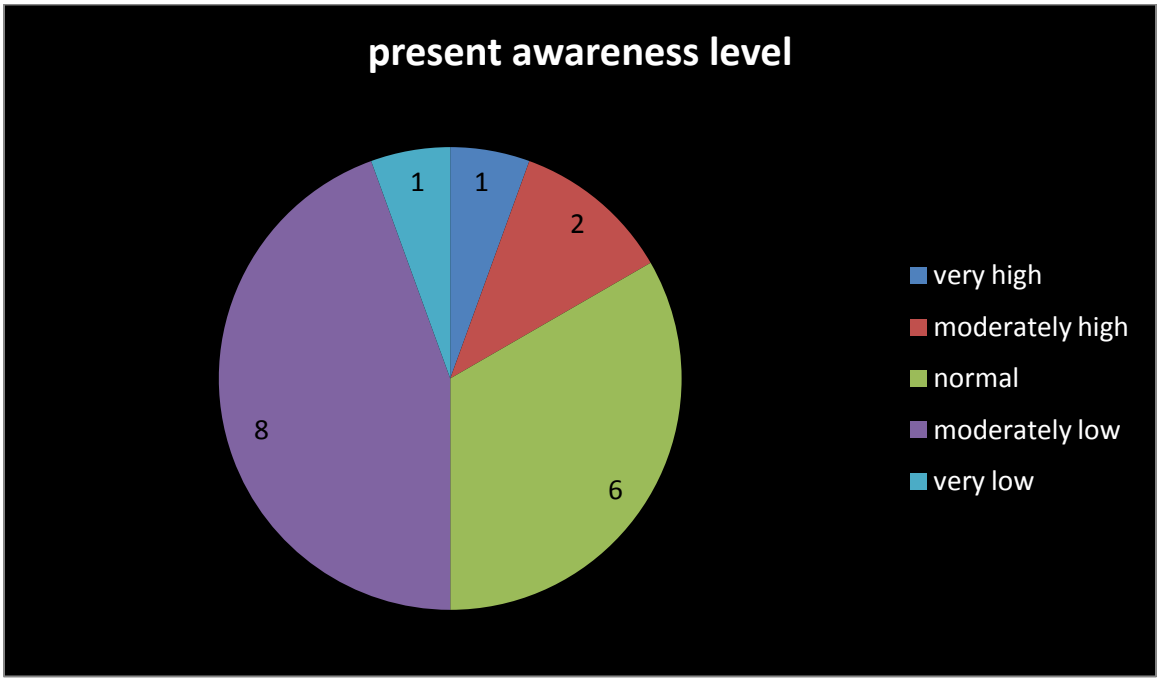
Verorab, kamreb and rabipure are widely used brands



Choice of brand is due affordability, availability ,quality and safety

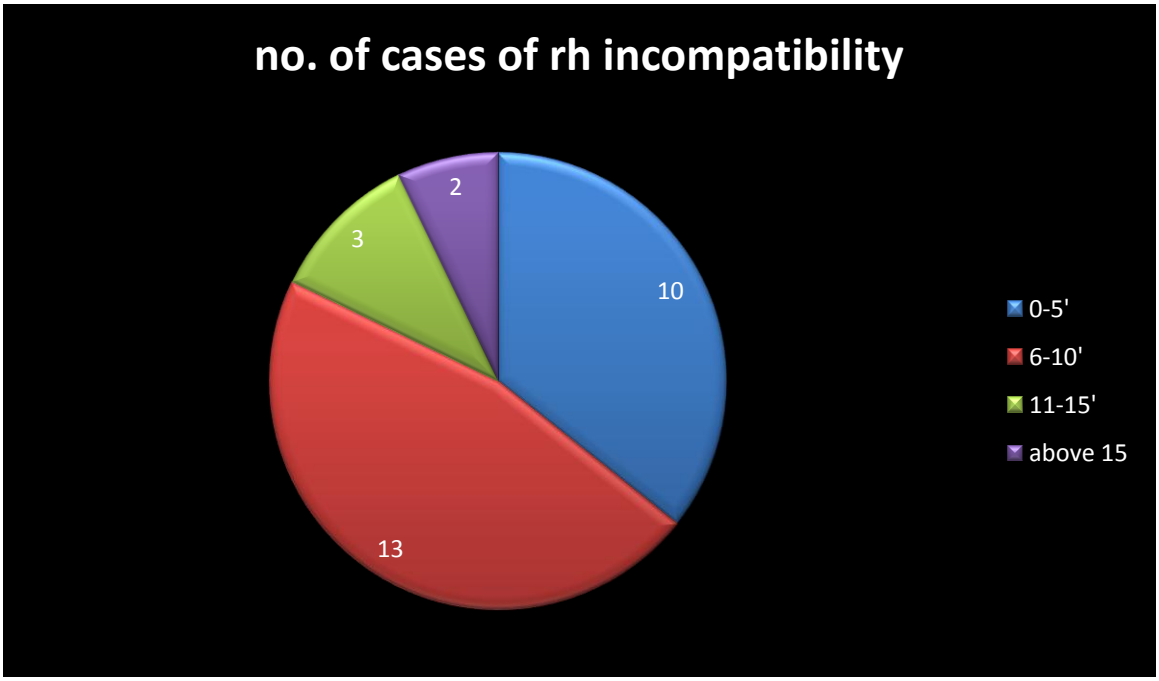


8 out of 20 doctors were satisfied with there brand

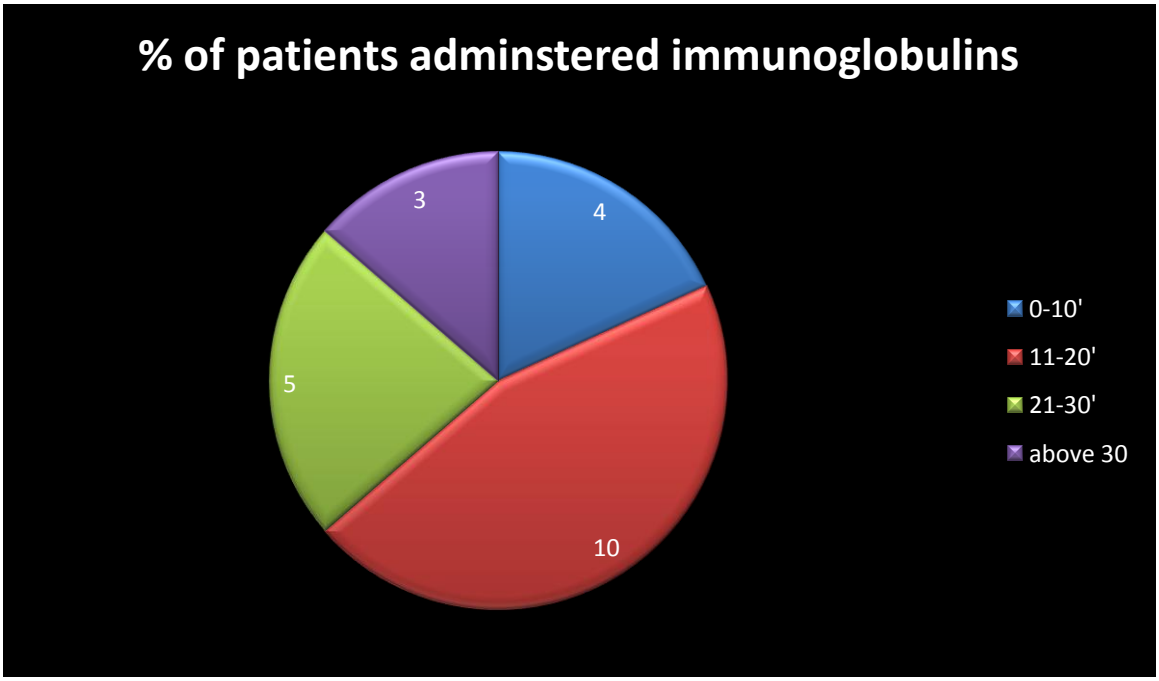


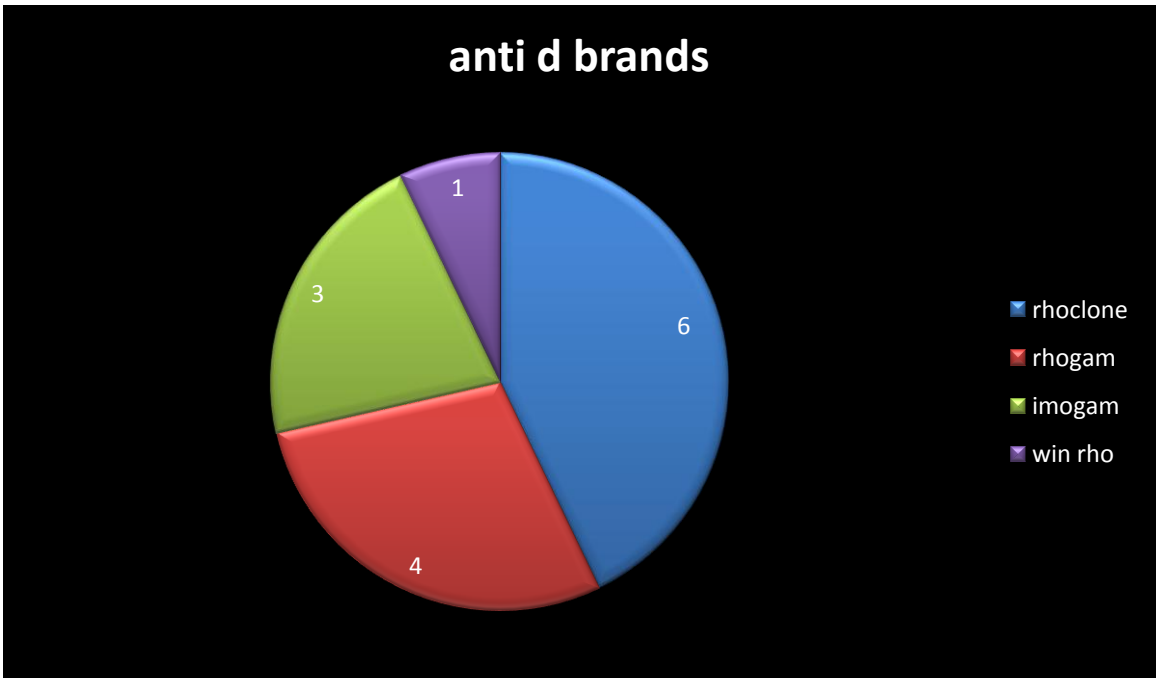
Awareness level is moderately low according to 8 respondents

Analysis of anti-d: 27 respondents

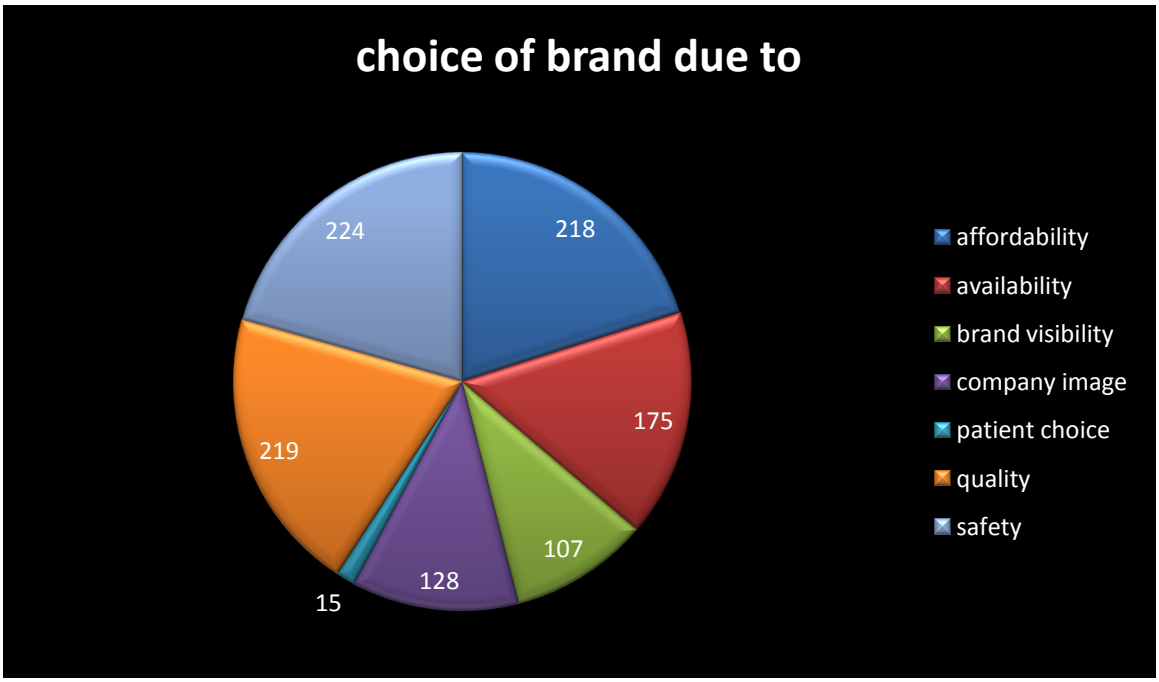


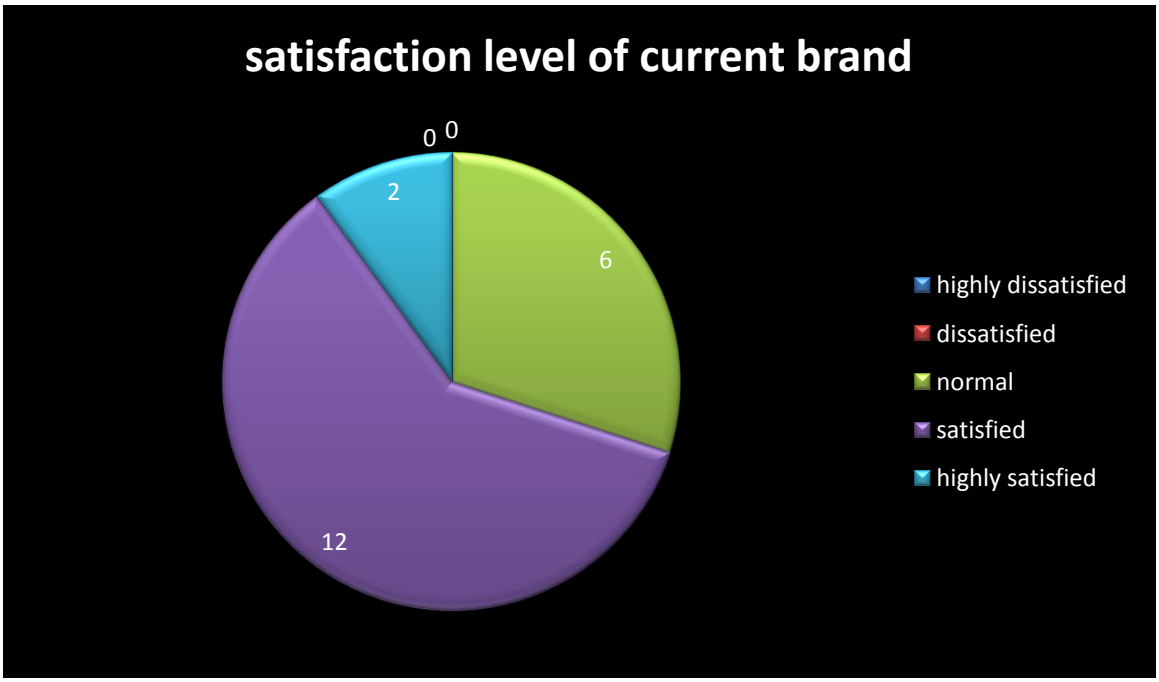
13 doctors were having patients 6-10 per month



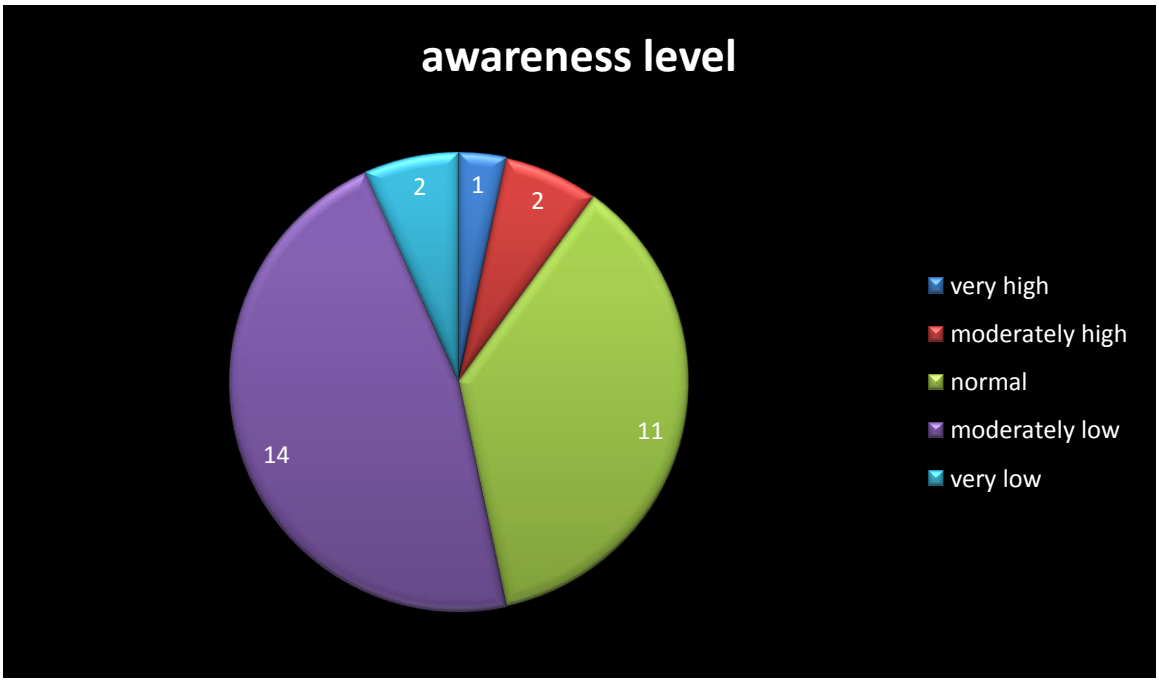


Rhoclone is a major brand of anti d



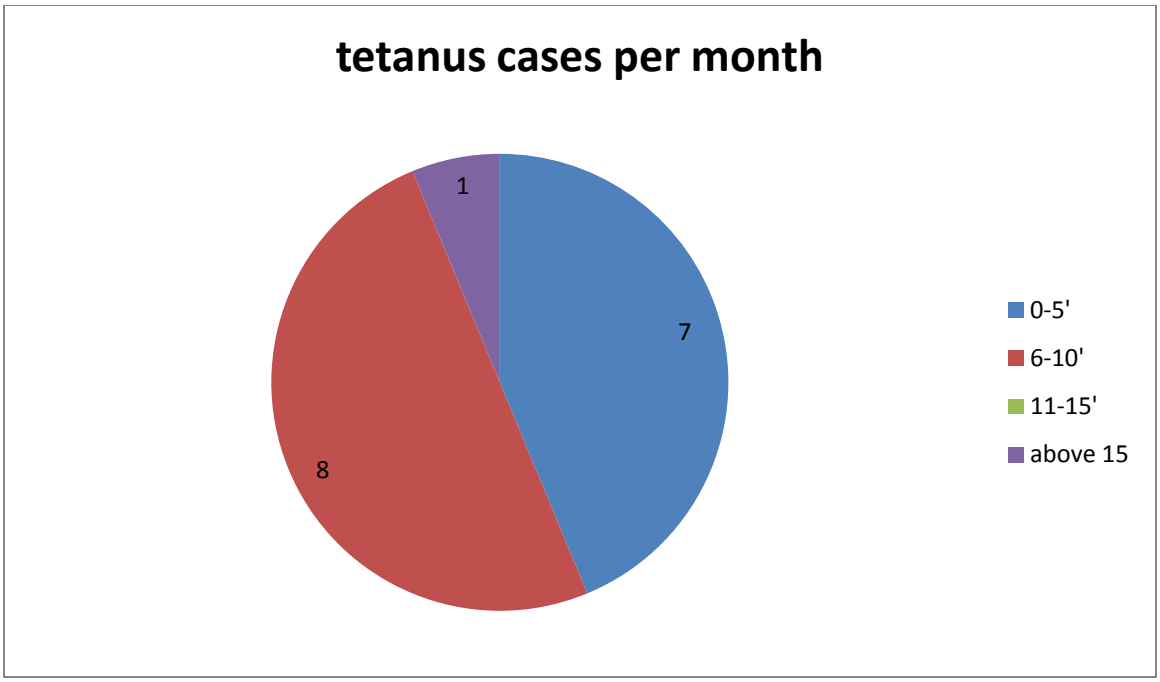


12 doctors out of 27 were highly satisfied

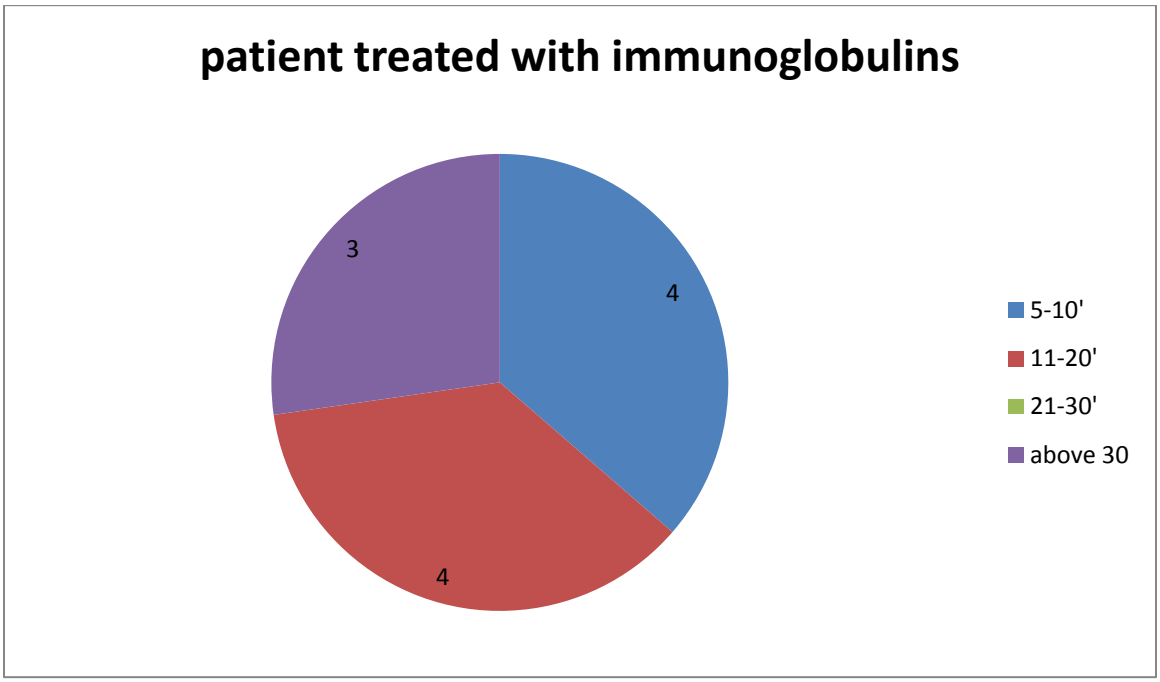


14 respondents agreed that there was lack of awareness

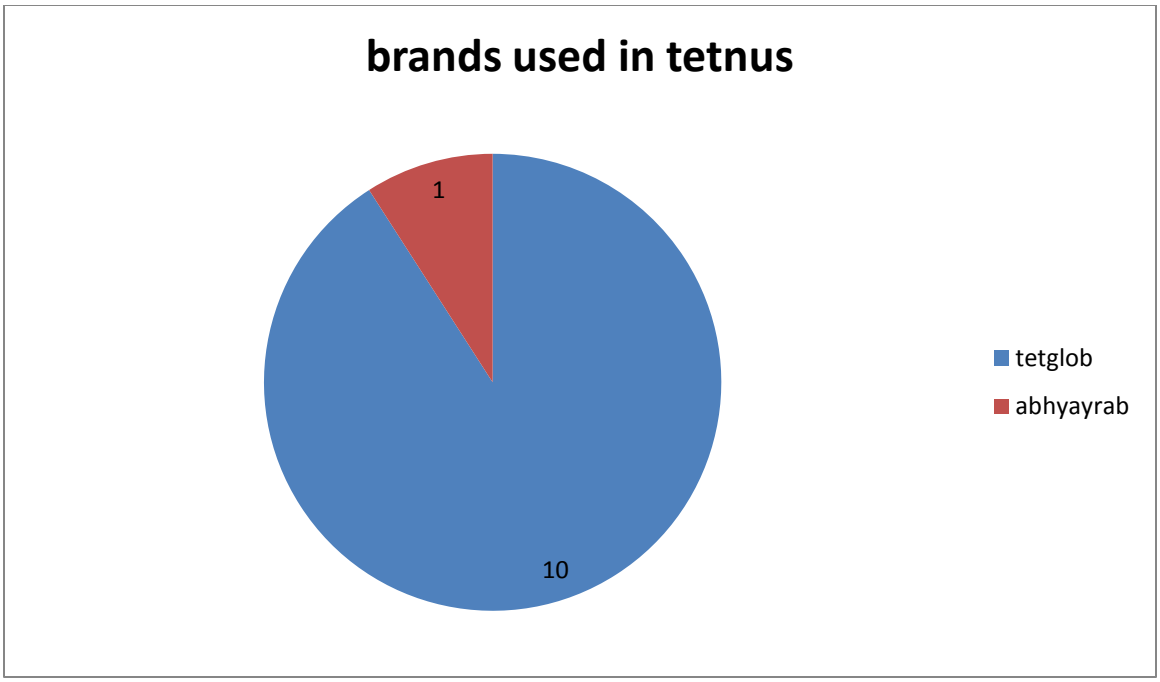
Analysis of tetnus: 18 respondents



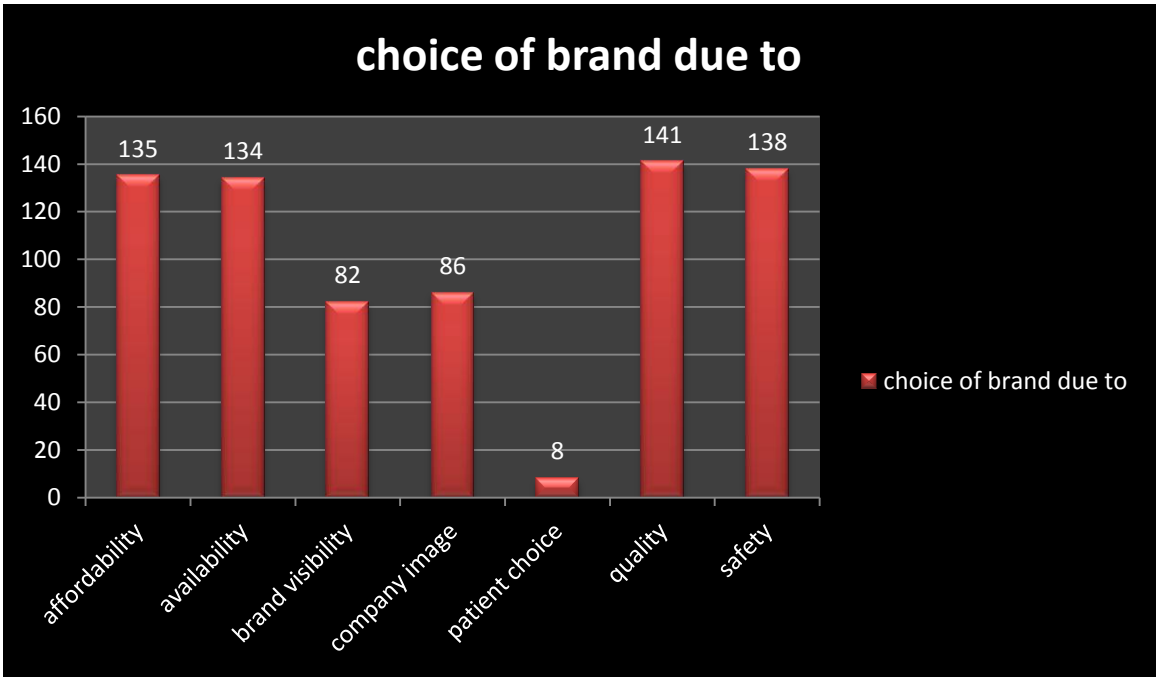
Out of 18, 8 doctors were examining 6-10 patients per month



3 of the doctors used ig in more than 30% of there patients



Tetglob is a clear cut market leader



Choice of brand is due to quality and safety

9 out of 18 doctors were satisfied with the current brand

6 respondents said that awareness was normal in there fraternity

Observation and findings:

- There is a huge opportunity for plasmahep in rajasthan. As it is not available yet in MUKHYAMANTRI FREE DRUG DISTRIBUTION SCHEME. There is a huge patient pool of hepatitis in gujrat and rajasthan
- There is a tender system in many of the hospitals of gujrat and rajasthan so there is huge opportunity for plasmahep
- Rest other products like immunoglobulins for tetnus, rabies and anti-d are freely available in rajasthan. But still the private practioners used to prescribe branded immunoglobulins and in private hospitals on demand these immunoglobulins are made available.
- As we see hepatitis there is less patient pool because from birth onwards vaccination is done,so very less patient are there of hepatitis
- Hepaglob and revace are major competitors of plasmahep.
- For doctors still the high cost of immunoglobulins is a barrier. Some doctors do not prescribe due to high cost. The awareness in small cities is still not upto the mark.
- In rabies verorab and rabipur are highest selling
- There is a huge patient pool of rh incompatibility. In every city gynae doctors were having great no. of patients of rh incompatibility
- Rhoclone is a major brand used in rh incompatibility
- In tetnus also there are huge no. patients. Tetglob is the market leader in this segment. It has largest market share

Conclusion:

It was found that the these immunoglobins products are very costly due to which sometimes doctors do not prescibe them. In rajasthan anti-d , rabies , tetnus immunoglobulins are freely available in government hospitals so the private companies has to struggle a lot to get the share from private hospitals. In gujarat many of the hospitals has tender system. As the health of people is improving day by day the patient pool is also very less .moreover the awareness level is also not upto the mark, there is a demand of health education and about these immunoglobulins. it was found that in there is great demand of anti-d. RH incompatibility is very common. So to bring a anti-d product would be a good option it will also increase the market share of the company. As the market has cut throat competition and to bring a anti-d there is risk also as in rajasthan there will be double competition because it is freely available in government hospitals In tetnus whole market is captured by tetglob, and in rabies case verorab is trying hard to gain the market share.