"Unravelling the Allergy Puzzle: Exploring the Link Between Serum IgE, Eosinophil Count, and ABO Blood Group in Young Healthy Adults"- a cross sectional study.

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Abstract

Background: The study done explores correlations between ABO blood groups, Serum IgE levels, and Absolute Eosinophil Counts in young adults, aiming to uncover predispositions to allergic manifestations. Understanding these connections can prompt early interventions to mitigate allergies, benefiting both individuals and society. No such study has been conducted in the northeastern region of India till now. **Materials and methods:** The study, conducted at Gauhati Medical College and Hospital, employed a cross-sectional design on healthy young adults aged 18-35. Methods included serum IgE estimation via ELFA, absolute eosinophil count determination using a direct method, and ABO/Rh blood grouping via slide hem-agglutination. Statistical analysis utilized ANOVA, t-test, and Pearson's coefficient of correlation. **Results:** The study involved 234 subjects, examining blood group distribution, gender, and age. Blood groups A, B, O, and AB constituted 38.88%, 40.17%, 15.81%, and 5.12% respectively. Gender distribution was 52.56% male and 47.43% female. Age groups ≤20, 21-30, and 31-35 represented 33.33%, 49.14%, and 17.52% respectively. Serum IgE and Absolute Eosinophil counts varied significantly among blood groups, with B group showing the highest levels. Non-O blood groups exhibited higher IgE and eosinophil counts compared to group O. There was no significant difference in IgE and eosinophil counts between genders. Positive correlations were observed between IgE and eosinophil counts across different age groups. **Discussion:** The study aimed to correlate serum IgE and absolute eosinophil count among ABO blood groups and genders in 234 healthy adults. Blood group B showed the highest susceptibility to allergic diseases. No gender disparity was noted. Positive correlations were observed between IgE levels and eosinophil counts across age groups. Further research is warranted. **Conclusion**: The study analyzed serum IgE and eosinophil count across ABO blood groups and genders. It highlighted associations with allergic disorders. Larger, longitudinal studies are recommended for better understanding and targeted interventions.
Key words: Serum IgE, Absolute Eosinophil Count, Allergic diseases, ABO blood group.

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INTRODUCTION

Antibodies are immunoglobulins (Ig) produced by B cells in response to foreign antigens. Originally defined as gamma globulins, immunoglobulins constitute fraction of plasma proteins because it was found that when they are subjected to electrophoresis, they were detected at the backsides of alpha and beta globulins probably due to their slow electrophoretic mobility. Subsequently, it was established that these gamma globulins are products of cells of immune system & so called immunoglobulins. Antibodies have two fundamental properties for defense against pathogens: they bind specifically to the antigen that is responsible for their induction by one part of their molecule & then dispose the captured antigen with the cooperation of other molecules like complements or phagocytes of the immune system. The primary structure of immunoglobulin consists of one polypeptide from two genes. Secondary structure of immunoglobulin consists of immunoglobulin fold. Tertiary structure consists of immunoglobulin domain and the quaternary structure is the immunoglobulin monomer.

Immunoglobulin E is a type of reaginic antibody which mediate acute & sometimes life threatening allergic reactions in atopic patients. IgE molecules have two heavy (epsilon) chains & two light chains. They have a molecular weight of 200 kDa, a sedimentation coefficient of 8.2S & they contain 12% carbohydrate.[1] Half-life of IgE is 2.4 days – shortest among all immunoglobulins. Their serum concentrations are in the range of 0.1-0.7 mg/L with a average being 0.3mg/L. Serum of patients suffering from asthma, hay fever, eczema, Wiskott-Aldrich syndrome & helminthic infestations have a higher concentration of IgE. IgE- forming plasma cells are found most commonly in the respiratory, gastric & intestinal mucosa & in regional lymph nodes but a few are noted in spleen & other lymph nodes. IgE antibodies are capable of sensitizing basophils & mast cells. In IgE molecule the Fc portion fits into specific receptor sites on the cell surface.[2] When bivalent or multivalent antigen bind to at least two IgE molecule, the mast cell or the basophils is triggered to degranulate, thereby releasing vasoactive substances, specially histamine & slow reacting anaphylaxis substances, which are responsible for such clinical manifestations as wheal & flare reactions, bronchospasm, small vessel dilation & shock. Reduction of the disulphide bonds destroys the ability of the IgE molecule to bind to Fc receptor & heating at 56 degrees centigrade inactivates its cytotropic activity. This inactivation is associated with loss of antigenic determinants in C-epsilon 3 & 4 domains, suggesting that these regions are important for binding to the receptor.[3] In early part of the 20th century it was recognized that IgE has unique properties among immunoglobulin isotypes in its ability to induce extremely rapid pathological responses & to act as a highly sensitive immunological amplifier. IgE provides the critical link between the antigen recognition role of the adaptive immune system & the effector functions of mast cells & basophils at mucosal & cutaneous sites of environmental exposure. These functions have made IgE an attractive target for pharmacological intervention with IgE blockade having clinical potential across many different therapy areas. The role of IgE in acute phase as well as delayed phase of allergic reaction due to constant expression of several mediators, cytokines & chemokines by activated mast cells & basophils has been established. In the early 1990's , the discovery of T- helper2 (Th2) lymphocytes, their role in controlling IgE production & in late phase of allergic inflammation reduced biological importance of IgE antibodies.[4] However, further researches

achieved decidedly important results regarding not only biological role of IgE but also therapeutic of IgE blocking monoclonal antibodies.[5] It marked the turning point in defining biological role of IgE & in 2003, the introduction of omalizumab, a humanized monoclonal antibody (mAb), that selectively binds to IgE, used for the treatment of moderate to severe persistent allergic asthma as well as chronic idiopathic urticaria marked a important milestone in both mAb & anti-IgE therapy. The coming decades are likely to witness further advances in our IgE biology, together with the introduction of newer anti-IgE therapies as well as formulation of innovative strategies to manipulate IgE axis and modulate allergic disease. The biological role of IgE is complex & related to its ability to influence the functioning of several immune & structural cells involved in the pathogenesis of chronic allergic inflammation. The biological pathways that IgE uses to influence cell activity rely on interactions with several receptors. Two classes of receptors have been identified: high affinity (FcεRI) receptors & low affinity CD23 (FcεRII) receptors. Mast cells, basophils, dendritic cells (DC's), airway smooth muscle cells (ASMC's), epithelial cells, endothelial cells & eosinophils express FcεRI receptors.[6,7,8,9] It has been found that IgE captures the allergens, facilitating their presentation to the Th2 lymphocytes.[10] FcεRI-IgE dependent allergen presentation by dendritic cells may critically lower the atopic individual's threshold to mount allergen specific T- cell responses.

There are 3 fundamental components of allergic reactions:

(i)Formation of allergen specific IgE;

(ii)Activity of mast cell caused by allergen re -exposure, which cross links Ig on the surface of mast cells, activating them to cause the signs & symptoms of an immediate hypersensitivity reaction.

(iii) Allergic inflammation, mediated primarily by recruitment & activation of eosinophils.

Each of these events involve cellular recruitment to the reaction site (called chemotaxis) along with activation of these cells to produce their products & altered cellular traffic to gather the cells together in an optimal fashion to promote allergic reaction.

Eosinophils were first identified in the late 19th century & eosinophilia has been known to be associated with a wide variety of conditions including asthma & atopic diseases.[11] The eosinophil was first described for its characteristic intracytoplasmic granules exhibiting a high affinity for the negatively charged dye, eosin. Eosinophils are mobile, terminally differentiated granulocytes that arise principally from the bone marrow. They are usually 8μm in diameter & nucleus is also usually bilobed. Eosinophils has large crystalloid granules which are secondary granules characterized by their coarse size and brick red in color when stained with acidic dyes such as eosin. On electron microscopy the crystalloid granules contain electron dense crystalline core surrounded by an electron-lucent granule matrix. Eosinophils also contain 4 other types of granules: primary granules, small granules, lipid bodies & small secretory vesicles.[12] Crystalloid granules are membrane bound & contain a number of highly cationic basic proteins which are implicated in tissue damage observed in asthma & other similar allergic conditions. Allergen & parasite induced eosinophils has been shown to be T-cell dependent and are mediated by soluble factors (cytokines) released from sensitized lymphocytes. Recent advances in human eosinophil research have also indicated that the eosinophilic infiltration into the tissue in allergic type responses & asthma are regulated by a series of biological events which includes a complex interplay between immunologic and

inflammatory mechanisms including cytokines & chemokines.[13] The relatively recent discovery of IL-5 in 1980,[14] its interaction with eosinophils and subsequent results of anti-IL-5 blocking mAb treatment in patients with asthma confirmed the importance of IL-5 in eosinophil mediated inflammation in humans.[15,16] Eosinophils both respond to and manufacture certain cytokines. IL-5 appears to be a major growth factor for eosinophils. IL-5 is also produced by Th2 cells further supporting the developing allergic cascade. Eosinophils can secrete many cytokines such as IL-3, GM-CSF, TNFα, and IL-1 when activated.[17] Any one of these cytokines or all of them serve to enhance and sustain the allergic inflammatory process by mast cell activation (IL-3) further eosinophil recruitment is done by TNFα whereas IL-1 altering the target tissue and even direct tissue damage. The activated eosinophils also produce and secrete multiple basic proteins and lipid mediators associated with allergic inflammation.[18] Inflammation has three major components: recruitment, where the inflammatory cells are drawn from the circulation under a direct chemical influence called chemotaxis; altered traffic, where the inflammatory cells are held at the site of developing inflammation; activation, where the inflammatory cells exert their influence e.g.: producing cytokines, lytic enzymes, phagocytosis etc.[19] In allergic inflammation, a combination of Th2 cells and mast cell activity appear to be most responsible for the initiation of eosinophilic activities. Activated mast cells secrete TNFα and therefore may directly influence recruitment of eosinophils. Once activated eosinophils are themselves a source of secreted TNFα which may serve to continue the recruitment of new eosinophils to the site of inflammation. Cytokines play a fundamental role in adhesion molecule expression. IL-1 acts on the endothelial cell to increase the expression of several adhesion molecules such as ELAM-1 (Endothelial leukocyte adhesion molecule), ICAM-1(Intercellular adhesion molecule) and VCAM-1(Vascular cell adhesion molecule). VCAM-1 expression may be the most important in allergic (eosinophilic) inflammation. VLA-4 is another molecule of importance as regards allergic reactions. This molecule is expressed on activated lymphocytes, mast cells, eosinophils. Thus, expression of VCAM-1 on endothelium (of say, the nose or lung) and VLA-4 on activated mast cells & eosinophils are necessary steps for eosinophilic infiltration of these organs in late phase of allergic reactions.

The human red cell membrane contains a variety of blood group antigens, which are also called agglutinogens**.** ABO is the major human blood group system – the distribution of which varies between countries. ABO blood groups are genetically transmitted through locus 9q34 of chromosome 9. The A and B antigens gets inherited as Mendelian dominants, and individuals are divided into four major blood types on this basis. Type A individual has the A antigen, type B has the B, type AB has both, and type O has neither antigen. The A and B antigens are complex oligosaccharides that differ in their terminal sugar. The ABO, H, Lewis blood group antigens are determined by the action of glycosyltransferases that attach sugar moieties to disaccharide on the red blood cells. The addition of fucose to these disaccharide precursors creates the H antigen & further modifications to the H antigen by glycosyltransferases leads to the synthesis of blood group antigens encoded by the ABO gene. The O allele does not produce any active enzyme & has α-fucose (1‣2) galactose disaccharides [O(H)structures] on its cell surface while in type A or B individuals the O antigen is capped by the addition of α-N- acetylgalactosamine or α-galactose residues, respectively. The A & B genes differ in a few single base substitutions that change four amino acid residues which may cause differences in A & B transferase specificity.[20] A critical single base deletion was found

in the O gene, which results in an entirely different, inactive protein incapable of modifying the H antigen. Saliva ABH secretor determination is based on testing for blood group antibodies in saliva. ABH secretors are identified by the secretion of ABO antigens in fluids such as saliva, sweat, tears & breast milk.[21] About 15% of people are ABH non-secretors. The secretor gene that encodes for 2α-L-fucosyltransferase and the ABO blood grouping system that codes for glycosyltransferases, act in concert to build up oligosaccharide structures in exocrine secretion systems, including the respiratory tract, playing a role in adhesion of environmental factors to epithelial cells. Glycosyltransferases are controlled by the ABO system to build oligosaccharide structures on the cell surfaces of erythrocytes & vascular endothelium, as well as in the exocrine secretion system including the respiratory tract. Alpha -2- fucosyltransferases *FUT1(H)* of red blood cells & vascular endothelium & *FUT2* (secretor positive) of the exocrine secretion system are structural genes that collaborate with glycosyltransferases. Studies based on separate analysis of the secretor & ABO systems have led to discordant results, probably because of the complexity of interactions between these genes. When a combined analysis of ABO blood groups & secretor phenotypes was performed a cooperative interaction between the two systems was described. Blood group O/ non -secretor subjects has lower lung function values & higher prevalence of atopy. The product of ABO & secretor genes seems to influence the adhesion of infectious agents thus having a modulator effect on viral & bacterial respiratory infection. Since the oligosaccharide composition of the cell membrane & mucosal secretions change with age and influence the adhesion of infectious agents, the age pattern of atopic diseases could reflect the interaction between cell maturation & oligosaccharide structure & its effect on susceptibility to bacterial and viral agent. The ABO blood group genetic locus has three alleles, which means three different forms of the same gene. These three alleles, I^A, I^B, and I^O, determine the three blood types. These alleles are typically called A, B, and O. The type O allele is either functionless or almost has negligible function, so it causes no significant type O agglutinogen on the cells. Conversely, the type B and A alleles do cause strong agglutinogens on the cells. Thus, the O allele is recessive to both the A and B alleles, which show co-dominance. From literature studies, it was observed that the O blood group phenotype is associated with allergic rhinitis in males. However, there has been no study conducted in this part of India to exhibit the relationship between ABO blood group, Serum IgE and Absolute Eosinophil count in respect of manifestations of allergic disorders.

Thereby, the main idea of the present study was to establish the existence of any correlation between Total Serum IgE level and Absolute Eosinophil Count with preponderance of developing allergic manifestations in ABO blood group individuals.

Serum IgE being the marker for Type 1 hypersensitivity reaction and absolute eosinophil count marks inflammatory process due to allergy – there are not many studies showing their relationship with ABO blood group so that in case of positive correlation necessary personal, environmental and therapeutic steps can be taken early to combat the allergic manifestations because my study population of young adults (18-35years) are in their most productive period of their life and can actively contribute to development of the society as a whole. So, if at all they are detected to have more of the allergic parameters-steps can be taken accordingly so that their proneness to allergy don't manifest into symptomatology and subsequent progression to the diseased state whereby they have to lose productive years of their life or have to go to a morbid condition in future. Moreover, no such type of study has been conducted in this part

of India to establish any relation of serum IgE and absolute eosinophil count with ABO blood group in respect of development of allergic manifestations and subsequently diseases. Therefore, the motive to do the study is to find out whether any particular blood group of ABO type has any preponderance to development of allergic manifestations as evidenced by rise of serum IgE level and increase of absolute eosinophil count.

MATERIALS AND METHOD

The study was conducted in the department of Physiology, Gauhati Medical College and Hospital. Ethical clearance was obtained from institutional ethical committee. The study is a cross sectional study. The study was carried out on young healthy individuals of Gauhati Medical College & Hospital, who met the inclusion criteria mentioned below and were willing to participate in the study. An informed consent was obtained from each patient prior to participation in the study. A proforma containing the necessary queries regarding the subject of the present study was given to each subject to fill up. Young healthy adults in the age group of 18-35 years were included in the study of either gender. Subjects without any major cardiovascular, respiratory, hematological and chronic allergic diseases were tested. Those who were not on any long term medication were included as well as individuals who were nonsmokers. Patients with known cardiovascular, respiratory or hematological diseases or with known history of allergic disorder were not taken in the study. Unwilling individuals who otherwise fulfilled the required criteria were left out. Pregnant women were not taken in the study. The sample size was calculated using the formula of $4pq/d^2$ where 'p' is the prevalence of the allergic diseases amongst the above mentioned age group, 'q' is 100-p and 'd' is the allowable error with respect to 'p' which is around 5-20% of 'p' in case of proportions as we have used parameters serum IgE, eosinophil count in relation or proportion to the ABO blood groups in the study population. As per these 234 healthy adults irrespective of gender were tested. With these outlook estimation of serum IgE was done as also estimation of absolute eosinophil count was done alongwith determination of ABO and Rh blood group.

ESTIMATION OF SERUM IgE:

PRINCIPLE

The assay principle combines a two-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA). The interior of the Solid Phase Receptacle (SPR) is coated during production with monoclonal anti-IgE immunoglobulin (mouse). Each SPR is identified by the IGE code. The SPR serves as the solid phase as well as the pipetting device for the assay. Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent strips. All of the assay steps are performed automatically by the instrument. The reaction medium is cycled in and out of the SPR several times.

First step: The sample is collected, and then transferred into the well containing alkaline phosphatase-conjugated anti-IgE antibodies. The sample/conjugate mixture is cycled in and out of the SPR several times to speed up the reaction. This operation also enables the IgE to bind with the immunoglobulins coated on the interior of the SPR and with conjugate to form a sandwich. Unbound components are eliminated during the washing steps.

During the final detection step, the substrate (4-Methylumbelliferyl phosphate) is cycled in and out of the SPR. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methylumbelliferone), the fluorescence of which is measured at 450

nm. The intensity of the fluorescence is proportional to the concentration of IgE present in the sample. At the end of the assay, results are automatically calculated by the instrument in relation to the calibration curve stored in memory, and then printed out.

BLOOD SAMPLING METHOD

Under all aseptic and antiseptic precautions, 5 ml of blood was collected by venipuncture in the cubital fossa and then transferred into a 3.2%(0.11 mol/l) trisodium citrate vial and centrifuged for fifteen minutes at 3000 rpm. The supernatant plasma obtained was collected and then transferred to a sterile vial and used immediately for estimation of serum IgE concentration or stored at 2-8^{0}C for a maximum of five days.

The estimation of Serum IgE concentration was done in MINIVIDAS machine.

CHEMICALS AND EQUIPMENTS USED FOR ESTIMATION OF SERUM IgE:

CHEMICALS

1. **Serum IgE kit**

CONTENT OF THE KIT– RECONSTITUTION OF REAGENTS

60 IGE strips	STR	Ready-to-use
60 IGE SPRs 2x30	SPR	Ready-to-use. Interior of SPR coated with mouse monoclonal anti-IgE immunoglobulins
IgE control 1 x 2 ml (liquid)	C1	Horse serum+ human IgE+ metacresol 1.4g/l. The confidence interval in KIU/l(International kilo units per litre) is indicated on the MLE card after the following mention: "Control C1 Dose Value Range".
IgE calibrator 1 x 2 ml (liquid)	S1	Horse serum + Human IgE+ metacresol1.4g/l. The titer in KIU/l is indicated on the MLE card after the following mention: "Calibrator (S1) Dose Value". The confidence interval in “Relative Fluorescence Value” is indicated on the MLE card after the following mention: "Calibrator (S1) RFV Range".
IgE diluent 1x 5 ml (liquid)	R1	Ready-to-use. Horse serum+ metacresol 1.4g/l

The Strip

The strip consists of 10 wells covered with a labeled, foil seal. The label comprises a bar code which mainly indicates the assay code, kit lot number and expiration date. The foil of the first well is perforated to facilitate the introduction of the sample. The last well of each strip is a

cuvette in which the fluorometric reading is performed. The wells in the center section of the strip contain the various reagents required for the assay.

Description of the Serum IgE strip

Wells	Reagents
1.	Sample well
2 - 3 - 4	Empty wells
5	Conjugate: alkaline phosphatase-labeled monoclonal anti-IgE immunoglobulins (mouse) + 0.9 g/l sodium azide (600 µL).
6 - 7	Wash buffer: Sodium phosphate (0.01 mol/l, pH 7.4) + 1 g/l sodium azide (600 µL).
8 9	Wash buffer: Di-ethanolamine (1.1 mol/l, or 11.9%, pH 9.8) + 1 g/l sodium azide (600 µL). Empty well
10	Cuvette with substrate: 4-Methyl-umbelliferyl phosphate (0.6 mmol/l) + diethanolamine(DEA) (0.62 mol/l or 6.6%, pH 9.2) + 1 g/l sodium azide (300 µL)

The Vidas serum IgE kit is stored at 2-8^{0}C. The reagents are not freezed, except for calibrators and controls after reconstitution. All unused reagents are stored at 2-8^0 C.

Equipment's

1. **MICROPIPETTE**: A micropipette of 100 µ liter measuring capacity was used during estimation of IgE.
2. **CENTRIFUGE MACHINE**: The centrifuge machine (REMI METALS GUJARAT) was used.
3. **MINI VIDAS MACHINE**: MINI VIDAS is a compact automated immunoassay system based on the Enzyme Linked Florescent Assay (ELFA) principles.

It is completely self-contained with an analytical module with 12 test positions / 2 independent 6 – test compartments along with an integrated monitor, keyboard and printer. It also has automated barcode identification.

4. Others:

Syringes: 5ml disposable syringes were used for withdrawing blood for estimation of Serum IgE.

Test tubes: Several test tubes were used for sampling, centrifuging and incubating blood and platelet poor plasma.

Tips

Disposable gloves

PROCEDURE:

One IgE strip and one IgE SPR was used for each sample, control or calibrator to be tested. Test code was entered by selecting the "IGE" on the instrument. The calibrator was identified by "S1" and tested in duplicate. The control was tested, by identifying it as "C1".

The calibrator, controls and samples were mixed using a Vortex-type mixer. 100 µL of calibrator, sample or control was pipetted using micropipette into the sample well. The SPRs and strips were inserted into the instrument. It was made sure that the color labels with the assay code on the SPR's and reagent strips matched.

The assay was initiated as directed in the Operator's Manual. All the assay steps are performed automatically by the instrument. The assay was completed within 30 minutes.

Results & Interpretation:

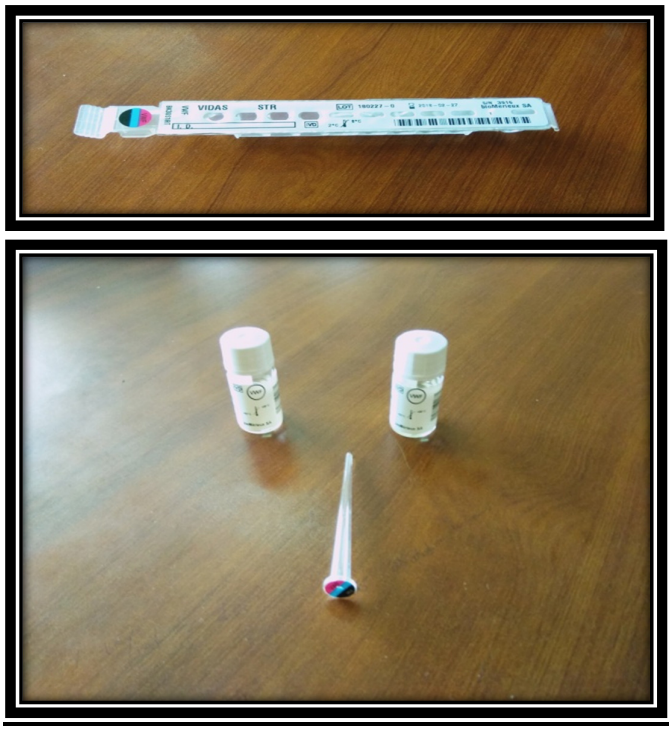
The results were analyzed automatically by the computer. The results were automatically calculated by the instrument by using calibration curves which were stored by the instrument. Concentrations were expressed as "KIU/l" (International kilo Units per litre)

Range of expected values:

Published studies show that it is difficult to determine "normal" values for IgE serum concentrations. The choice of the sample is very important. Furthermore, the circulation of IgE is brief, as their lifespan is short. As a guideline, 80% of the values corresponding to a non-atopic population are less than 150KIU/l

Apparatus for estimation of Serum IgE levels

Mini VIDAS machine



IgE Estimation Kit

Centrifuge Machine

ESTIMATION OF ABSOLUTE EOSINOPHIL COUNT:

Absolute Eosinophil Count was determined by Direct method.

Principle:

In the direct method a volume of blood is diluted 20 times in a WBC pipette with a special diluting fluid which stains the eosinophils along with its granules and removes the RBC's & other WBC's. The eosinophils present in the volume of the diluted blood is counted and from it the number of eosinophils present in one cubic mm of undiluted blood is calculated out.

Apparatus and reagents:

Compound Microscope
WBC pipette
Hemocytometer slide with Improved Neubauer Counting Chamber
Filter paper
Petridish
Sterile disposable needle/ Lancet
Cotton
Rectified spirit
Pilot's solution contains:(Each 100 ml of solution)

- Phloxine B (1% aqueous): 10ml (stains only eosinophil granules)
- Propylene Glycol: 50 ml. (Solvent for stain and lyses RBC's)
- Sodium carbonate (1% aqueous solution): 1ml (to enhance the staining of the eosinophil granules)
- Heparin: 100 units. (Anticoagulant)
- Distilled water: up to 100 ml (Solvent and lyses all WBC's except eosinophils which seems more resistant than other WBC's in this respect)

Procedure:

All the glasswares-WBC pipette, Hemocytometer slide with Improved Neubauer chamber were cleaned thoroughly. Subject's left ring finger was sterilized by rubbing with sterile cotton wool soaked in rectified spirit and allowed to dry. Then the finger was pricked with a sterile disposable needle and a free flow blood was obtained and it was sucked exactly upto 0.5 mark in a WBC pipette. Immediately after that the diluting fluid (Pilot's Solution) was sucked upto 11 mark. The blood was thoroughly mixed up with the fluid by gently rotating the pipette for at least 2-3 mins. We place a moistened filter paper in a petridish and keep the filled pipette covered with it so as not to allow evaporation of fluid to occur. The WBC pipette with the solution is allowed to remain in the moistened atmosphere for 15 minutes. The petridish is removed and then mix again and the first few drops were discarded and the counting chamber of the Improved Neubauer slide was charged with diluted blood.

The eosinophils are counted in four WBC squares after focusing under high power of the compound microscope. The eosinophils are seen as light orange with coarse brick red granules and nuclei.

Calculation:

Let the total number of eosinophils counted in all the four WBC counting chambers be =x
The depth between the counting area and the cover slip is 1/10 mm
Volume of 4 WBC counting squares is ~1x1x 1/10 cubic mm.

= 2/5 cubic mm

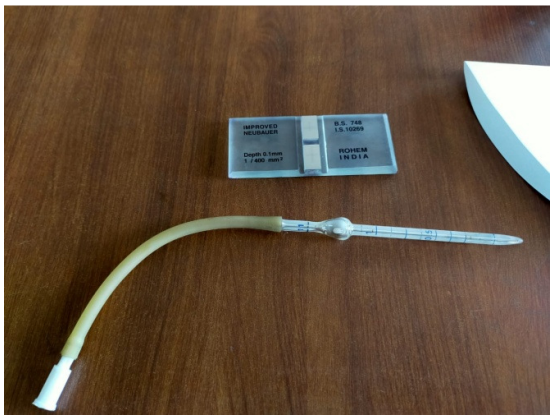
Dilution factor =20

So, 2/5 cubic mm of diluted blood contains = x number of eosinophils
∴ 1 cubic mm of diluted blood contains =5/2x number of eosinophils
∴ 1 cubic mm of undiluted blood contains= 5/2x X 20 number of eosinophils

= 50x number of eosinophils.

Normal range of absolute eosinophil count 40-440/ cubic mm of blood.

Apparatus used for Absolute Eosinophil Count



Haemocytometer slide with improved Neubauer counting chamber plus WBC pipette

Eosinophil counting fluid: Pilot's Reagent

Compound Microscope

ESTIMATION OF ABO AND Rh BLOOD GROUPING

The ABO and Rh blood groups were determined by the conventional slide hem- agglutination test.

Principle: Red cells contain different types of agglutinogens while plasma contains agglutinins. The red cells of the subject are allowed to react with commercially made

agglutinins. The presence or absence of the clumping of red cells in different agglutinins determines the blood group.

Apparatus and reagent:

- Antisera- high titer anti A and anti B sera

Anti Rh (D) for Rh determination

- Normal saline (0.9%)
- Three microscopic slides
- Test tubes with test tube rack
- Capillary pipette
- Applicator sticks
- Sterile and disposable pricking needles
- Spirit with cotton swab
- Compound microscope

Procedure: Slide method of haemagglutination

Preparation of red cell suspension

2-3 drops of blood were collected with aseptic precautions, by pin pricking the tip of left ring finger, in a small serologic test tube containing 2 ml of normal saline. The cells are allowed to settle down by keeping the tube erect and still. The tube is shaken a few times to prepare a uniform cell suspension.

Determination of ABO and Rh blood groups:

One drop each of commercially prepared anti-serum A, anti-serum B and anti-serum D was taken in a clean, grease free glass slide. Another drop of isotonic saline was also placed on the other side as control. The slide was accordingly labeled as anti A, anti B, anti D and control.

The red cell suspension was drawn from the bottom of the test tube by a dropper and a drop of it was added to each of the drops on the slide. The two were mixed with the help of separate applicator sticks. After 10 minutes the slide was gently rocked back and forth and examined for the presence of agglutination. The findings were confirmed under the low power of a compound microscope.

Interpretation: If there was agglutination the RBCs appear as massed together in clumps and lose their outline. If there was no agglutination the RBCs remain separated and evenly distributed. The blood group was determined as indicated in the table below:

Data Management and Statistical Analysis:

A daily maintenance of the filled in proforma was done for completeness and consistencies. All the data were entered into Microsoft excel software for proper analysis and computation. The data was presented as mean ± standard deviation**.**

Statistical analysis was done using the Analysis of variance (ANOVA), Unpaired t-test and Pearson coefficient correlation in the SPSS version 20 and Microsoft Excel software. P-value of < 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS: A total of 234 subjects were taken for the study after proper history- taking and clinical examination.

Blood Group	No. of Subjects	Percentage
A	91	38.88
B	94	40.17
O	37	15.81
AB	12	5.12

Table 1: Sample distribution of Subjects according to Blood Groups

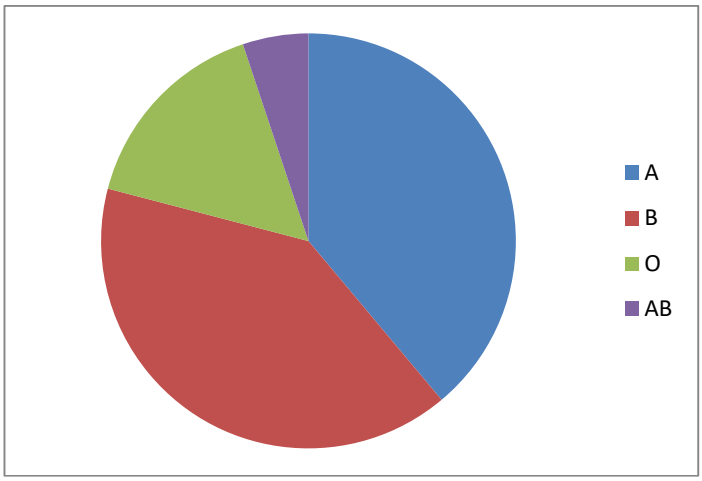


Fig 1: Pie chart showing percentile distribution of subjects according to different Blood Groups

Interpretation: From Table 5.1 we see that the sample distribution of subjects in A blood group was 91 (38.88%), B blood group was 94 (40.17%), O blood group was 37 (15.81%) and AB blood group was 12 (5.12%).

Gender	No. of subjects	Percentage
Male	123	52.56
Female	111	47.43

Table 2: Sample distribution of subjects according to Gender

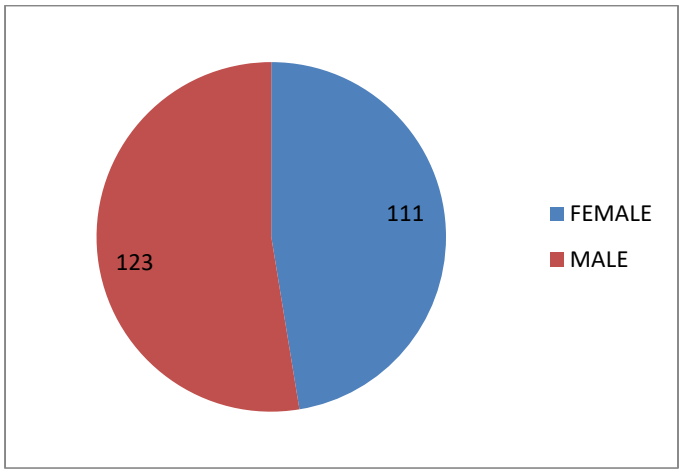


Fig 2: Pie chart showing percentile distribution of subjects according to Gender
Interpretation: From Table 5.2 we see that the sample distribution of subjects in male was 123 (52.56%) and female was 111 (47.43%).

Age group(years)	No. of subjects	Percentage
≤20	78	33.33
21-30	115	49.14
31-35	41	17.52

Table 3: Sample distribution of Subjects according to different age groups

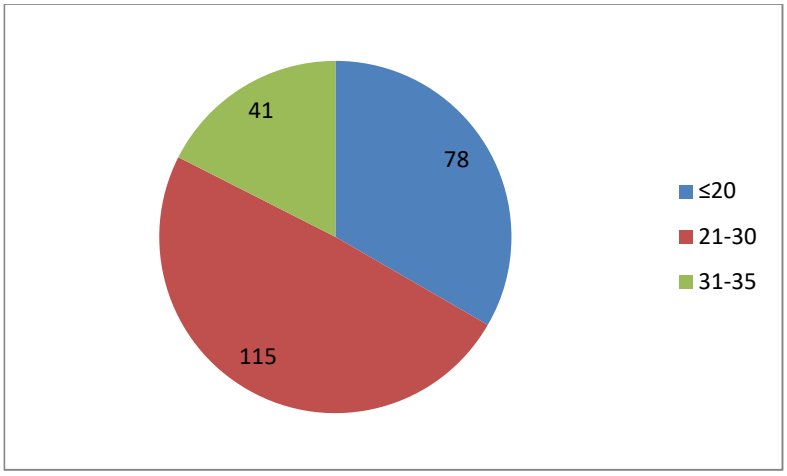


Fig 3: Pie chart showing percentile distribution of subjects according to different age groups

Interpretation: From Table 5.3 we see that the sample distribution of subjects in age group of ≤20 was 78 (33.33%), 21-30 years was 115 (49.14%), and 31-35 years was 41 (17.52%).

Age group(years)	Group	Mean age(years)	Standard deviation
≤20	I	19.48	0.51
21-30	II	25.32	3.22
31-35	III	33.07	1.43

Table 4: Mean age distribution of subjects among the different age groups

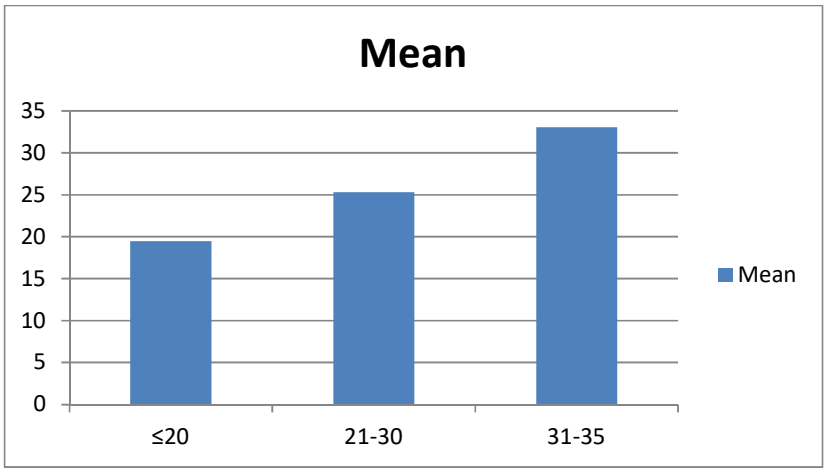


Fig 4: Bar diagram showing mean age distribution among subjects of different age groups.

Interpretation: From Table 5.4 we see that the mean age with standard deviation for group I was 19.48±0.51; for group II was 25.32±3.22; and for group III was 33.07±1.43.

Blood Groups	Serum IgE (IU/ml) Mean ± std	Absolute Eosinophil Count (cells/µL of blood) Mean ± std
A	254.13±37.23	130.02±27.96
B	541.94±35.32	246.64±28.62
O	156.81±30.31	156.51±25.35
AB	256.08±24.15	140.08±33.03

Table 5: Mean distribution of Serum IgE levels and Absolute Eosinophil count among different blood groups

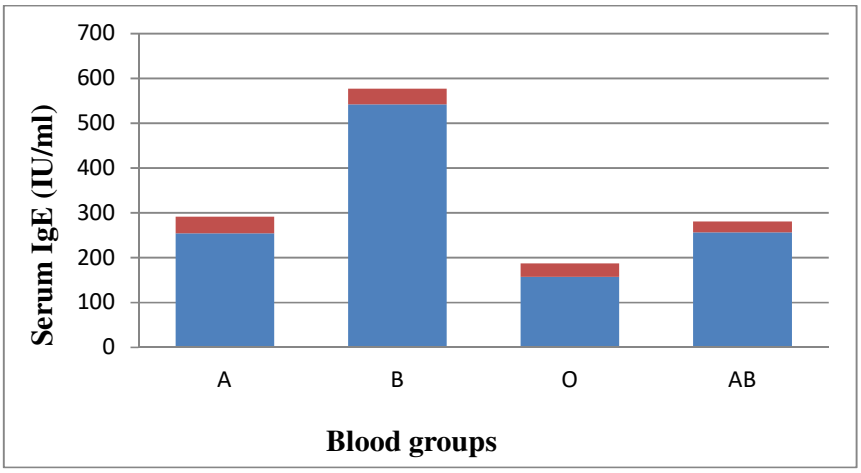


Fig 5a: Bar diagram showing mean distribution of Serum IgE levels among different blood group

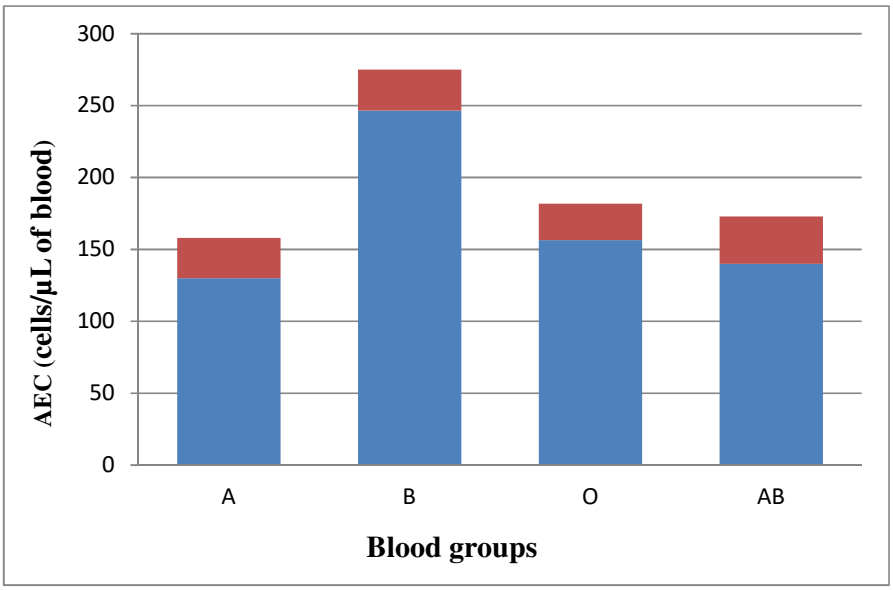


Fig 5b: Bar diagram showing mean distribution of Absolute Eosinophil count among different blood groups

Interpretation: From Table 5.5 and Fig 5.5a and 5.5b we see that the mean Serum IgE levels with standard deviation for blood group B was the highest (541.94±35.32 IU/ml) followed by blood group AB (256.0824.15 IU/ml) ; blood group A (254.13±37.23 IU/ml) and was lowest in blood group O (156.81±30.31 IU/ml). Also, the Absolute Eosinophil Count for blood group B was highest (246.64±28.62 cells/µL) as compared to blood group O (156.51±23.35 cells/µL of blood); blood group AB (140.08±33.03 cells/µL of blood) and blood group A (130.02±27.96 cells/µL of blood) respectively.

Blood Groups	Serum IgE(IU/ml) Mean± std	Absolute Eosinophil count(cells/µL of blood) Mean± std
O	156.81±30.31	156.51±25.35
Non O	391.58±148.42	186.28±64.47

Table 6: Mean distribution of Serum IgE levels and Absolute Eosinophil count among 'O' and non 'O' blood groups

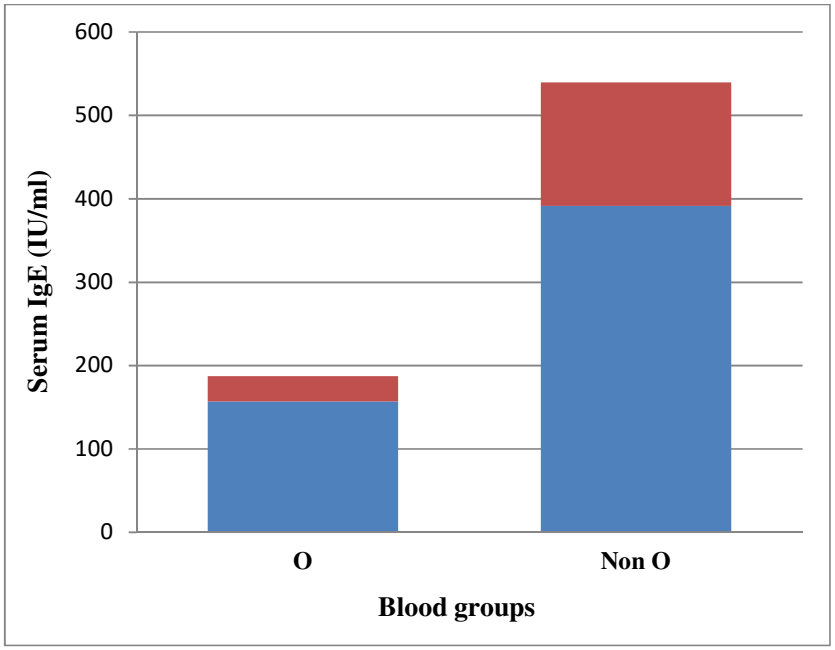


Fig 6a: Bar diagram showing mean distribution of Serum IgE levels among O and non O blood group

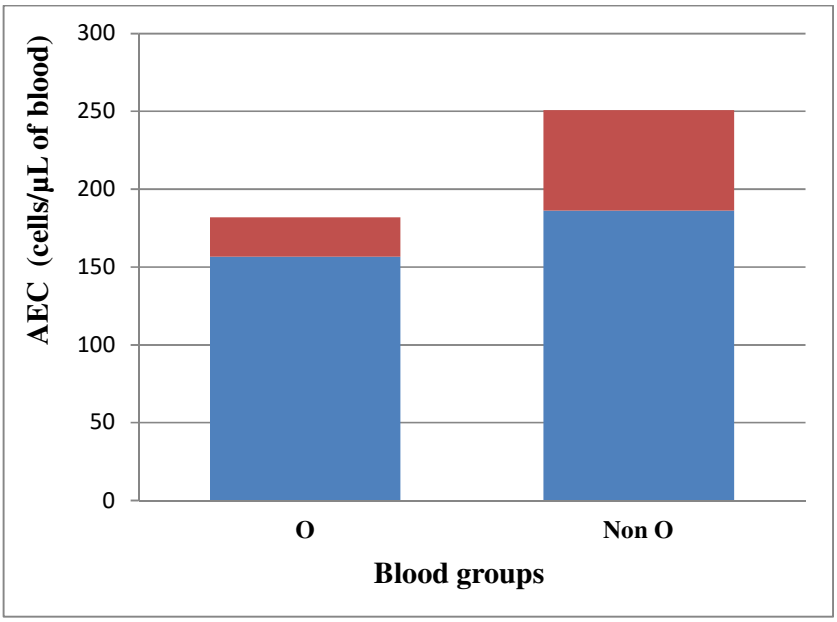


Fig 6b: Bar diagram showing mean distribution of Absolute Eosinophil count among O and non O Blood Groups

Interpretation: From Table 5.6 and Fig 5.6a and 5.6b we see that the mean Serum IgE levels with standard deviation for Non O blood group was the highest (391.58±148.42 IU/ml) as compared to O blood group (156.81±30.31 IU/ml). Also, the Absolute Eosinophil Count for non O blood group was higher (186.28±64.47 cells/µL of blood) as compared to O blood group (186.28±64.47 cells/µL of blood)

Gender	Serum IgE(IU/dl) Mean± std	Absolute Eosinophil count(cells/µL of blood) Mean± std
Male	360.47±169.06	179.67±60.71
Female	347.79±152.71	183.68±61.41

Table 7: Mean distribution of Serum IgE levels and Absolute Eosinophil count among male and female

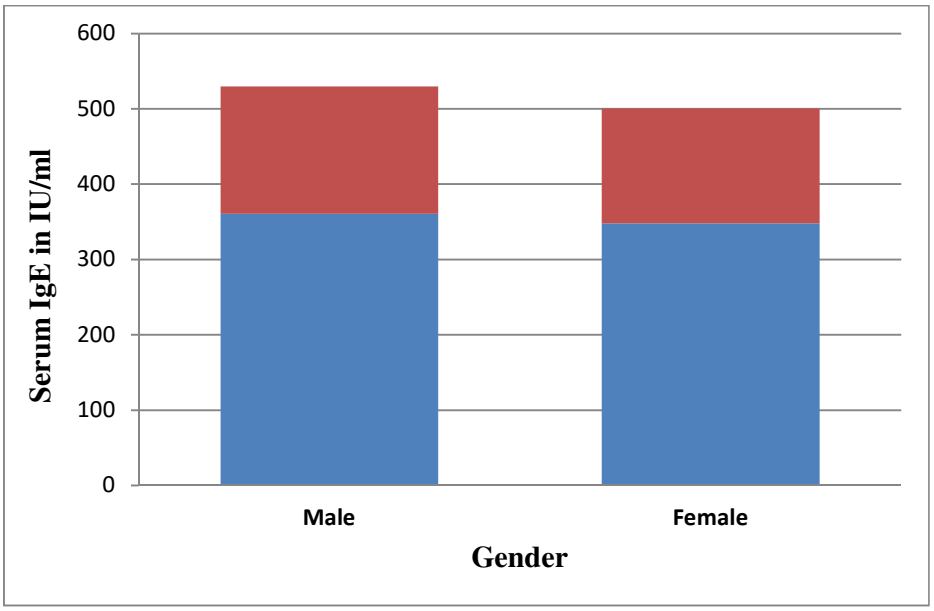


Fig 7a: Bar diagram showing mean distribution of Serum IgE levels among male and female

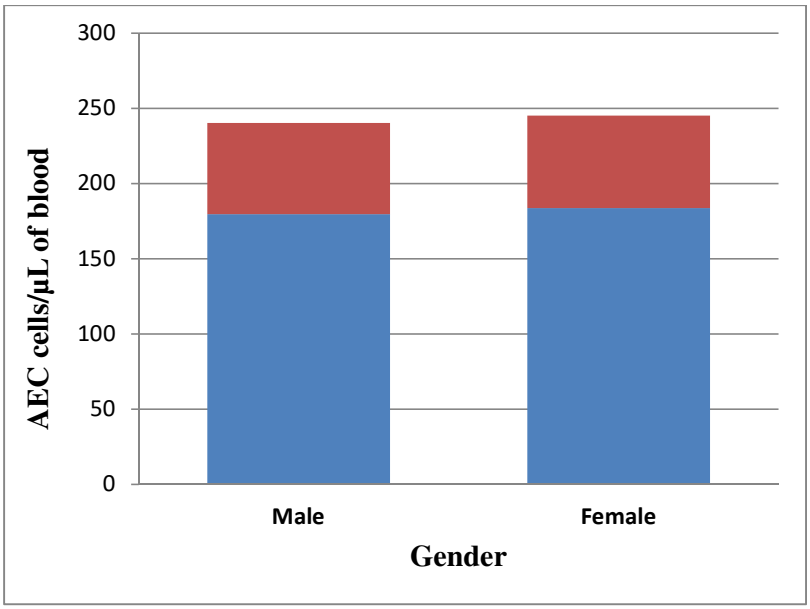


Fig 7b: Bar diagram showing mean distribution of Absolute Eosinophil count among male and female

Interpretation: From Table 5.7 and Fig 5.7a and 5.7b we see that the mean Serum IgE level with standard deviation for male was 360.47±169.06 IU/ml which was a bit higher than for female which was 347.79±152.71 IU/ml. The Absolute Eosinophil count for male was 179.67±60.71 cells/µL of blood and for female was 183.68±61.41 cells/µL of blood

Age groups (years)	IgE(IU/ml) Mean± std	AEC(cells/µL of blood) Mean± std
≤20	358.51±163.26	184.85±58.67
21-30	351.06±161.91	179.91±60.54
31-35	342.03±155.94	172.51±66.38

Table 8: Mean distribution of IgE levels and Absolute Eosinophil count among different age groups

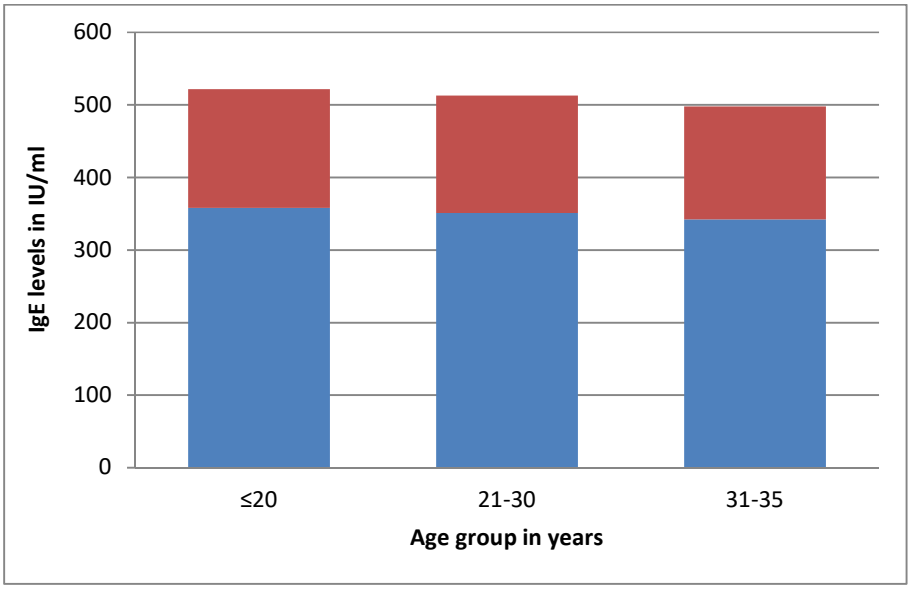


Fig.8a: Bar diagram showing mean distribution of IgE levels among different age groups

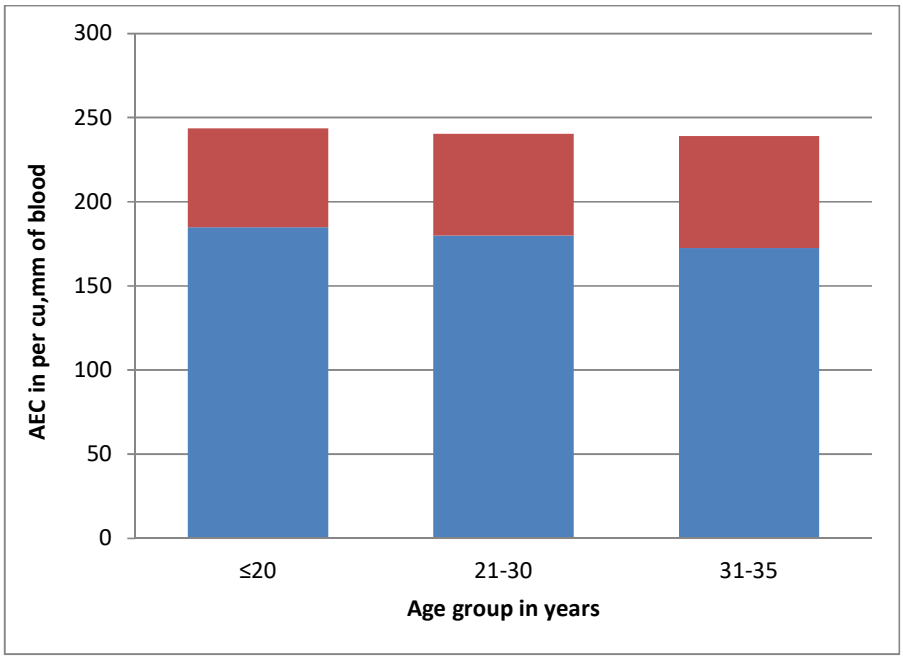


Fig 8b: Bar diagram showing mean distribution of Absolute Eosinophil count among different age groups

Interpretation: From Table 5.8 and Fig 5.8a and 5.8b we see that the mean IgE levels with standard deviation was highest in the age group ≤20 years i.e. 358.51±163.26 IU/ml followed by age group 21-30 with IgE levels of 351.06±161.91 IU/ml and age group 31-35 with 342.03±155.94 IU/ml. The Absolute Eosinophil count for age group ≤20 years was the highest (184.85±58.67 cells/µL of blood) as compared to the age group of 21-30 years (179.91±60.54 cells/µL of blood) followed by age group 31-35 years (172.51±66.33 cells/µL of blood)

Analysis of mean Serum IgE levels and Absolute Eosinophil count with different parameters:

To compare the mean Serum IgE and Absolute Eosinophil count among different parameters we used Analysis of variance (ANOVA) and Unpaired t-test to test the statistical significance of Serum IgE and Absolute Eosinophil count and to correlate the relationship between Serum IgE and Absolute Eosinophil count among different parameters Pearson's coefficient correlation (r) was used.

Parameters	**A Blood Group**	**B Blood Group**	**O Blood Group**	**AB Blood Group**	**df**	**p-value**
Serum IgE (mean± std in IU/ml)	254.13±37.23	541.94±35.32	156.81±30.31	256.08±24.15	3	<0.01*

Absolute Eosinophil count (mean± std in cells/μL of blood)	130.02±27.96	246.64±28.62	156.51±25.35	140.08±33.03	3	

*p-value<0.05 as significant value

Table 9: Analysis of variance of IgE and Absolute Eosinophil count among different blood groups

Interpretation: From Table 5.9 it was observed that the Serum IgE and Absolute Eosinophil count were significant (p-value <0.05) among the blood groups and B blood group showed significantly increased Serum IgE levels compared to other blood groups. Also, the Absolute Eosinophil count in B blood group showed a significant (p-value <0.05) higher value when compared with the other blood groups.

Parameters	O Blood Group	Non O Blood Group	df	p-value (two -tail)
Serum IgE (mean± std in IU/ml)	156.81±30.31	391.58±148.42	231	<0.01*
Absolute Eosinophil count (mean± std in cells/μL of blood)	156.51±25.35	186.28±64.47	139	<0.01*

*p-value<0.05 as significant value

Table 10: Unpaired t-test of Serum IgE levels and Absolute Eosinophil count among O and non O blood group

Interpretation: From Table 5.10 it was observed that the Serum IgE was significantly increased (p-value <0.05) among non O blood group as compared to the O blood group. A similar outcome with significant increased (p-value <0.05) absolute eosinophil count in non O blood group as compared to O blood group was observed.

Parameters	Male	Female	df	p-value (two-tail)
IgE (mean± std in IU/ml)	360.47±169.06	347.79±152.71	232	0.54
Absolute Eosinophil count (mean± std in cells/μL of blood)	179.67±60.71	183.68±61.41	229	0.61

*p-value<0.05 as significant

Table 11: Unpaired t-test of Serum IgE levels and Absolute Eosinophil count among the gender

Interpretation: From Table 5.11 it was observed that both Serum IgE and Absolute Eosinophil count was not significant among the male and female (p-value >0.05).

Parameters	≤20 Years	21-30 Years	31-35 Years	df	F-value	p-value
Serum IgE(mean± std in IU/ml)	358.51±163.26	351.06±161.91	342.03±155.94	2	0.143	0.866
Absolute Eosinophil count (mean± std in cells/µL of blood)	184.85±58.67	179.91±60.54	172.51±66.38	2	0.554	0.575

*p-value<0.05 as significant value

Table 12: Analysis of variance of serum IgE and Absolute Eosinophil count among different age groups

Interpretation: From Table 5.12 it was observed that the levels of Serum IgE and AEC were not significant (p-value >0.05) among the different age group.

Blood group	r -value	p-value
A	0.02	0.79
B	0.05	0.63
O	-0.24	0.15
AB	-0.29	0.36

*p-value<0.05 as significant value

Table 13: Pearson Correlation of Serum IgE levels and Absolute Eosinophil count among different blood groups

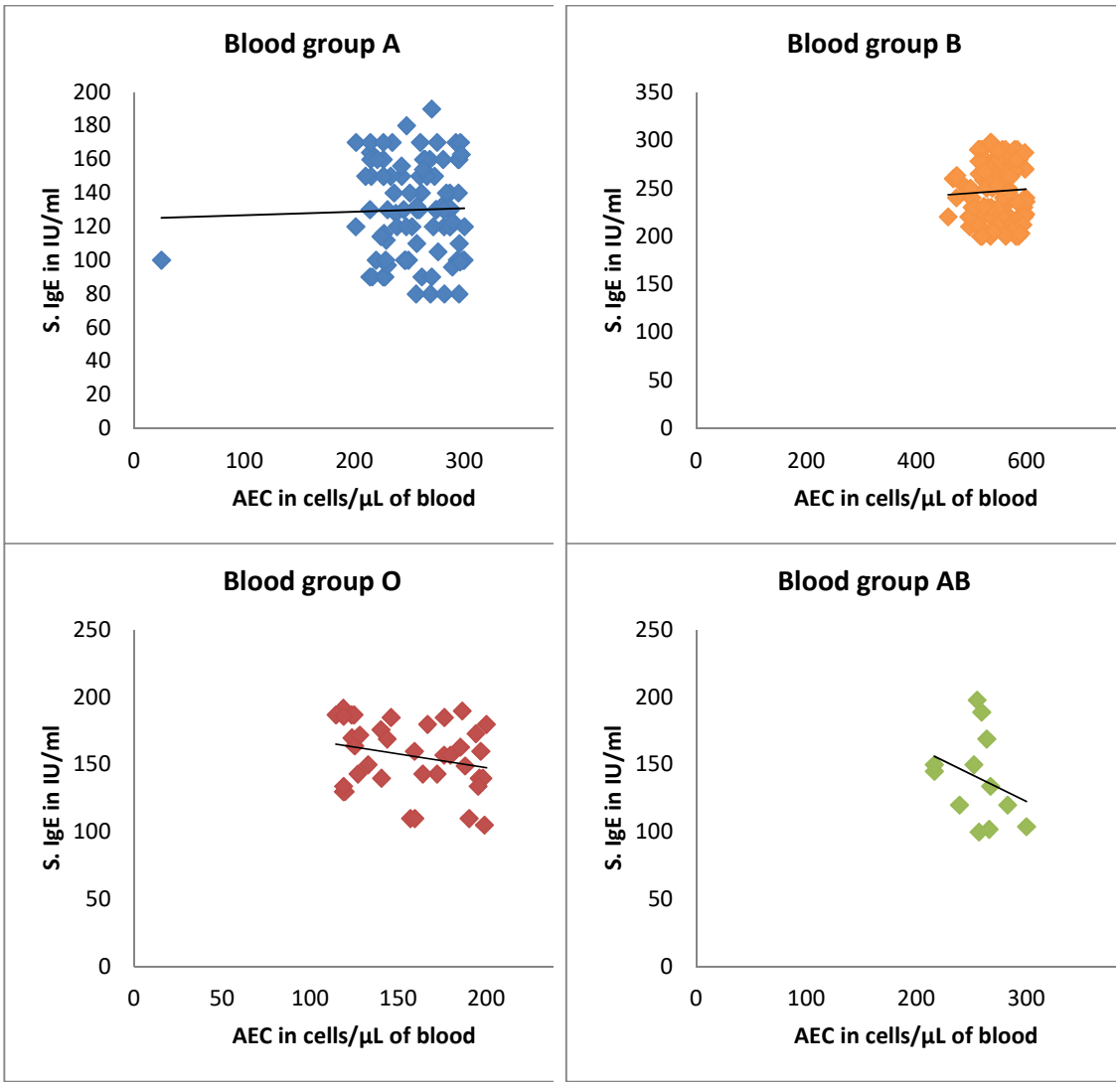


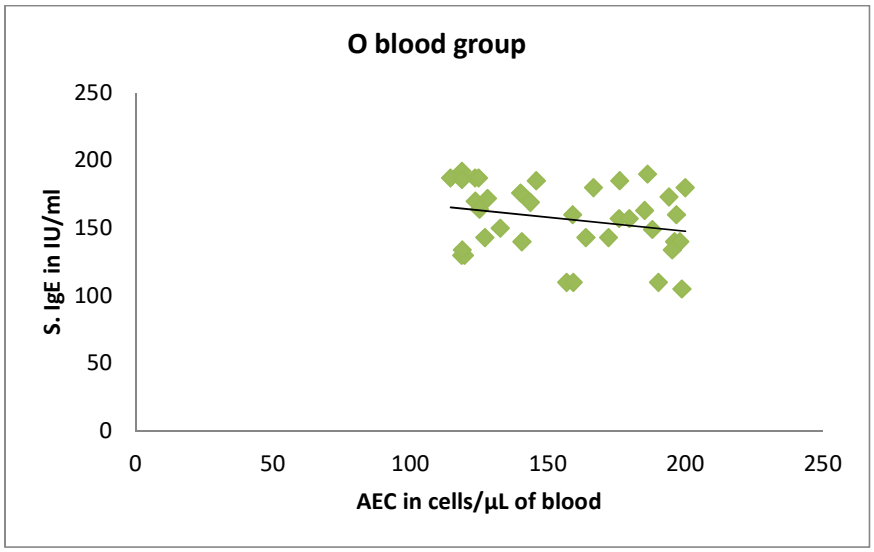
Fig 9: Scatter diagram showing correlation of Serum IgE and Absolute Eosinophil count among different blood groups

Interpretation: From Table 5.13 and Fig 5.9 it was observed that there was a slight positive correlation between Serum IgE and Absolute Eosinophil count in A and B blood group with no significant correlation ($p>0.05$). O and AB blood group showed a negative correlation between Serum IgE and Absolute Eosinophil count with no significant correlation ($p>0.05$).

Blood group	r -value	p-value
O	-0.24	0.15
Non O	0.87	<0.01*

*p-value<0.05 as significant value

Table 14: Pearson Correlation of Serum IgE levels and Absolute Eosinophil count among O and non O blood group.



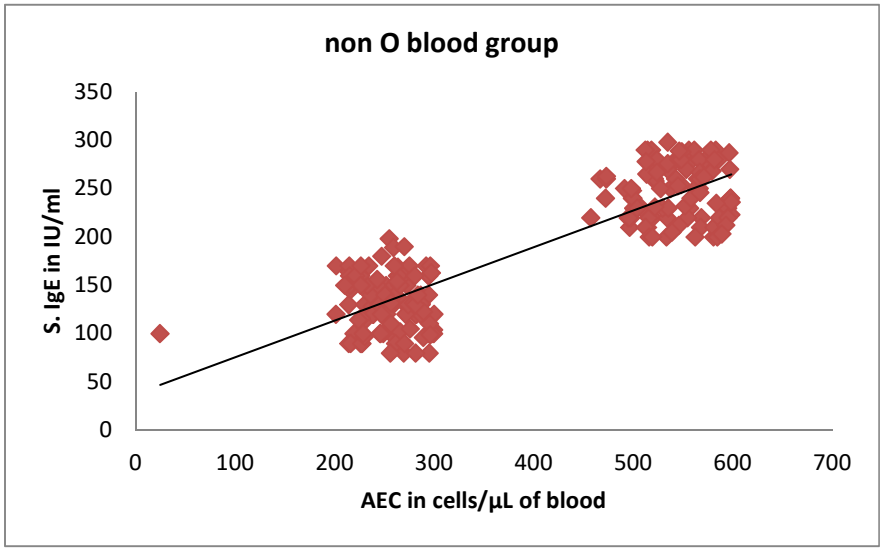


Fig 10: Scatter diagram showing correlation of Serum IgE and Absolute Eosinophil count among O and non O blood groups

Interpretation: From Table 5.14 and Fig 5.10 it was observed that there was a negative correlation between Serum IgE and Absolute Eosinophil count in O blood group but not significant ($p>0.05$). However, in non O blood group a significant positive correlation ($p<0.05$) was seen i.e. as the Serum IgE level increased there was a significant increase of the Absolute eosinophil count in non O blood group.

Gender	r –value	p-value
Male	0.81	<0.05
Female	0.81	<0.05

*p-value<0.05 as significant value

Table 15: Pearson Correlation of Serum IgE levels and Absolute Eosinophil count among gender

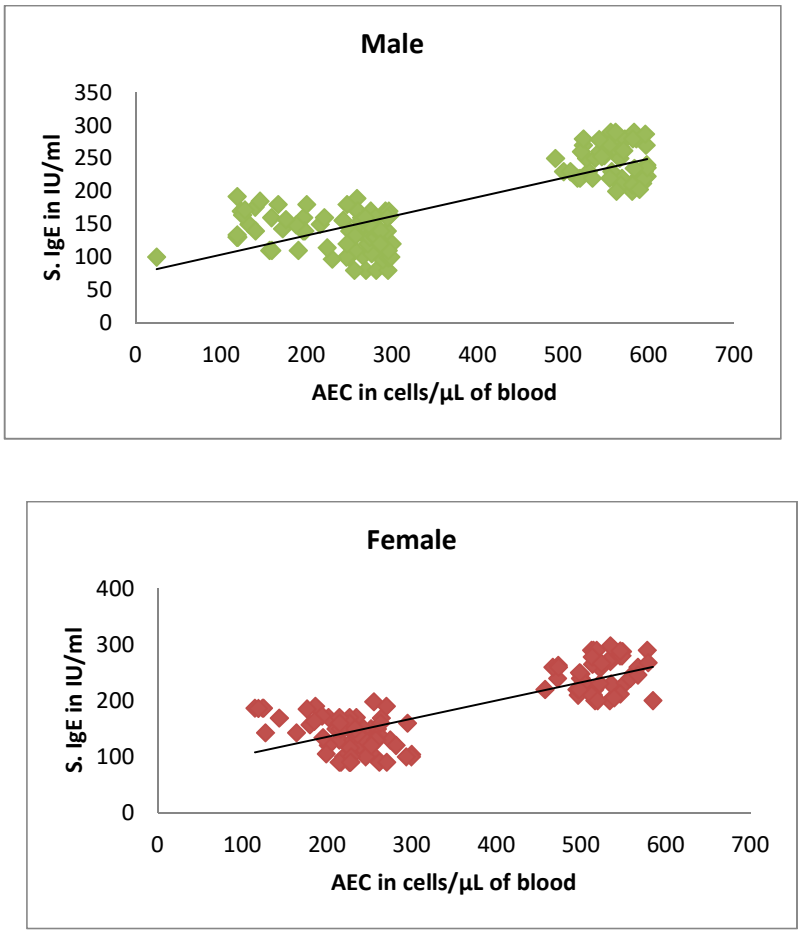


Fig 11: Scatter diagram showing correlation of Serum IgE and Absolute Eosinophil count among gender

Interpretation: From Table 5.15 and Fig 5.11 it was observed that there was a strong positive correlation between Serum IgE and Absolute Eosinophil count in male and female. A significant correlation ($p<0.05$) was seen among both male and female i.e. as the Serum IgE level increased there was a significant increase in the Absolute Eosinophil count.

Age group(years)	**r-value**	**p-value**
≤20	0.81	<0.01*
21-30	0.78	<0.01*
31-35	0.82	<0.01*

*p-value<0.05 as significant value

Table 16: Pearson Correlation of Serum IgE and Absolute Eosinophil count among different age groups

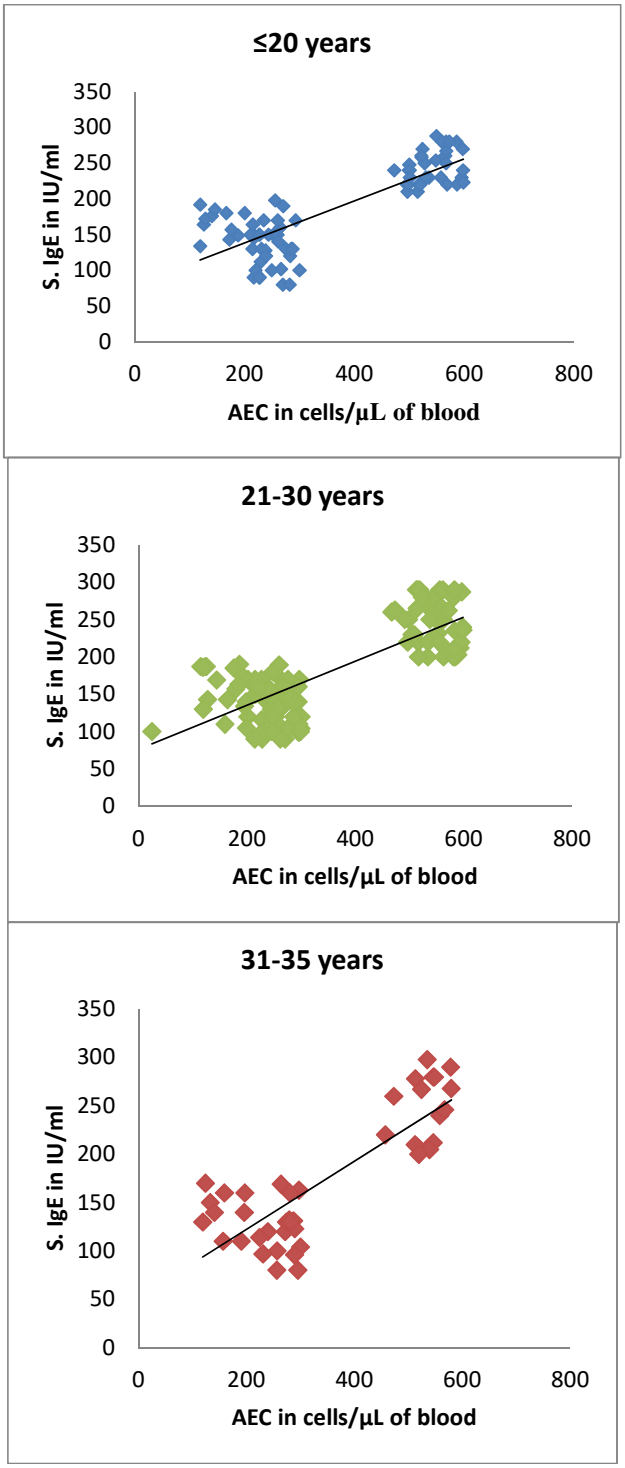


Fig 12 : Scatter diagram showing correlation of S. IgE and Absolute Eosinophil count among different age groups

Interpretation: From Table 5.16 and Fig 5.12 it was observed that there was a positive correlation between serum IgE and absolute eosinophil count among individuals of age group between ≤20, 21-30, 31-35 years respectively. Moreover, a significant positive correlation ($p<0.01$) was seen among all three age distribution groups of ≤20, 21-30, 31-35 years i.e. as the serum IgE level increased there was a significant increase in the absolute eosinophil count among those groups.

DISCUSSION:

M. Amarasekara in 2011 stated in his article that the discovery of IgE was done by Prausnitz & Kustner in 1921 & only after four decades in 1967- it was identified as an immunoglobulin subclass by Ishizaka & co-workers.[22] In 1968, WHO international reference centre for immunoglobulin announced the presence of fifth immunoglobulin isotype IgE.[23] IgE is the antibody isotype that contains the ε (epsilon) heavy chain & it is monomer with five domains in the immunoglobulin structure. It is normally present in plasma at a concentration of less than 1µg/ml & has a half-life of about 2 days in serum.[24] A new unit KU/L or IU/ml was introduced to express the level of IgE in peripheral blood to alleviate the inconvenience in expressing the very low levels of serum IgE- one KU/L is equal to2.4 ng/ml.[25] Once produced the IgE – binds to its receptor FcεR- which are of 2 main types: High affinity receptors(FcεRI) ~ are found on a wide variety of cells – Platelets, Basophils, Mast cells, Antigen presenting cells & monocytes, on the other hand low affinity receptors (FcεRII)- are found to be expressed on B-cells,[26] monocytes[27] & dendritic cells.[28] The role of high affinity receptors in the pathogenesis of allergy is well understood.[29,30]The biological role of low affinity receptors is still unclear.

Role of IgE in health & disease: IgE was discovered for its involvement in allergic reactions (Type 1 Hypersensitivities). People who have tendency to develop symptoms –when exposed to allergens ~produce IgE specific to that allergen- which evokes a cascade of reactions.[31] It has been shown that the dominant role of IgE – is to protect the host from parasitic infections – especially helminthic infections.[32] So it is believed that IgE has evolved to protect the humans from helminthic infections which once was the major threat for survival of human species.[33,34]

Role of IgE in helminthic infections: IgE plays a vital role in the cross talk between innate & adaptive immunity. Helminths are large parasites – that cannot be engulfed by phagocytes & could be best dealt by cytotoxic cells. Invasion of tissues by helminths- stimulates an autoimmune response – which generates a cytokine that shifts the TH_o cells to mature along the TH_2 pathway. These TH_2 cells- secrete interleukin (IL-4) which induces the B- cells to switch the immunoglobulin class to IgE. At the same time secreted IL-5 enhances the production & maturation of eosinophils.[35] IgE molecules coat the parasite which enables the tissue mast cells & circulating eosinophils to bind via IgE receptors. This interaction of IgE with their receptors – initiates a cascade of reactions in these cells which results in release of histamine & other toxic substances to their exterior. [36]

IgE in allergic reactions: In allergic reactions there is production of IgE antibodies – in response to allergen- then binding of IgE to F_c receptors of mast cells then after that –cross linking of the bound IgE by the allergen upon re-exposure after which occurs release of mast cell mediators such as histamine, lipid mediators, cytokines. Some mast cell mediators cause rapid increase in vascular permeability & smooth muscle contraction – with the end result that many symptoms occur. People with genetic predisposition – called atopics – have a personal tendency to develop IgE- when exposed to otherwise harmless environmental allergens. Such individuals have a allergen specific IgE (sIgE)- in their serum reflecting their exposure to allergens in the past.

Levels of Total IgE and sIgE: Rising trends of allergic diseases in affluent populations – in developed countries was alarming.[37] Investigations were carried out to find out the markers

of allergy in such populations. High levels of tIgE- allergic individuals –compared to healthy controls – lead to a identifying cut off level of tIgE- for a diagnosis of allergy. It was observed that –probability is very high in predicting allergy when the tIgE level is above 200KU/L.[38, 39] Longitudinal studies have demonstrated that levels of IgE increases with age from birth-regardless of the atopic status –but the increment in atopic children is abrupt & continue to have high levels in adulthood.[40, 41] Since most somatic IgE is bound by its receptors serum IgE may not necessarily reflect the systemic IgE levels. However, Dehlink & co-workers have been able to demonstrate that the level of serum IgE correlates well with cell bound IgE.[42] The pool of IgE in an individual is the sum of IgE produced against different allergens –i.e., specific IgE. Presence of sIgE in serum indicates that the individual has been exposed to the allergen earlier (sensitized). Presence of sIgE against a particular allergen above a level of 0.35 KU_A/L –is deemed positive for that allergen. [43] A person is said to be atopic if laboratory data shows a positive test. It should be noted that a positive result does not always correlate well with clinical feature of a person.

IgE levels in the in the population in tropics: In people living in helminth endemic areas of tropics –serum levels of tIgE are very high in such people despite being non-atopic.[44, 45] Indeed it is observed that the tIgE levels – are several folds higher in them –compared to atopic people in the developed western countries emphasizing the limited use of tIgE-as a marker for allergen in tropics. It is known that – helminths are capable of inducing IgE synthesis markedly. Analysis of IgE molecules in such people has revealed – that most of IgE are nonspecific.[46 , 47] It is postulated that – polyclonal synthesis of IgE – is a mechanism of the parasite – to evade host immune response

against it. The mechanism of immune evasion by helminths is not well elucidated to date. The observation of tIgE & low sIgE levels in populations in tropics is interesting & needs to be explored since it reflects some of the facts related to the control of IgE synthesis. Lynch et al reported that helminths enhance polyclonal synthesis of IgE resulting in high tIgE levels – while downregulating the production of sIgE. This suggests that control of tIgE & sIgE is independent from each other. Direct evidence for this comes from the study done by Sunyer & colleagues-which showed that tIgE levels are associated with asthma even in subjects negative to sIgE to common aeroallergens. It should be noted that the population for the latter study comes from an area not endemic for helminth infections. Reinforcing this notion- genetic studies have revealed different genetic loci for tIgE & sIgE profiles.[48, 49]

Elevated tIgE in other diseases: Presence of high levels of tIgE in allergic diseases is well documented. Nevertheless, there are other situations where an increase in level is observed. Hyper IgE syndrome, IgE myeloma, some disorders of vasculitis, though rare, should be considered in differential diagnosis for extremely high tIgE levels.

Therapeutic Implications: The cornerstone of an allergic reaction – is the cross linking of IgE molecules- bound to mast cell receptors. Recombinant monoclonal humanized antiIgE has demonstrated promising results as a treatment for asthma in adults. Further studies are needed to evaluate – long term safety & efficacy in the treatment of allergic diseases –with antiIgE treatment in children.

Paparo SB et al found out that high IgE levels in patients affected by Psoriasis and found that the concomitance of psoriasis & high IgE levels in the same patient possibly associated to allergies, should not come as a surprise anymore because both diseases are characterized by an

immunological disorder- involving cytokines & other inflammatory mediators – with massive activation of CMI by radio immunologic methods. It was concluded that – patients of severe psoriasis had high levels of IgE so it was concluded that IgE's have an important role in pathogenesis of psoriasis & atopic dermatitis – but the mechanism is not yet clear.

Elango Krishnan et al studied the prevalence of raised IgE levels & AEC in bronchiolitis in children aged 10 months – 2 years in tertiary care hospital stated that bronchiolitis is defined by a constellation of clinical symptoms & signs including viral upper respiratory prodrome – followed by increased respiratory effort & wheeze in less than 2 years old child.[50] Many viruses cause bronchiolitis with RSV being common. RSV affects children less than 1 year of age with 2-8 months being peak. Some prospective study has suggested that RSV infection predisposes to blood eosinophilia & airway hyperactivity leading to development of wheeze. Overproduction of cytokines released by T helper 2 lymphocytes – is responsible for illness especially interleukin 4 & 5. Interleukin 4 & 5 – cause migration of eosinophil & also increases IgE production.[51] Prevalence of increased AEC (28.1%) were correlated with age & is found to have high statistical significance. Prevalence of IgE in bronchiolitis (38.5%) did not have any statistical significance.

Clara Carpegianni in 2011 the association of blood group "O" in allergic rhinitis which affected around 600 million people worldwide. As allergic rhinitis is an atopic disease that have significant impact on the quality of life & the prevalence has increased abruptly in recent years in most western countries. The disease –also known as hay fever or pollinosis- occurs in individuals with a sensitized immune system. The allergen triggers the production of IgE antibodies – which bind to mast cells & basophils containing inflammatory mediators such as histamine, which are then released into the blood stream. Complex multifactorial allergic disease with environmental & genetic components. One hypothesis – to explain the steep rise in allergic diseases in recent years is the hygiene hypothesis: the excessive 'cleanliness' of the environment has led to a decline in the infectious stimuli that are necessary in the development of the immune system. Many other factors have been suggested to play a role in the development and expression of atopic diseases including changes in lifestyle, pollution, dietary changes with diminished nutritive value and stress. The strongest risk factors in the development of allergic symptoms are a family history of allergies, second hand cigarette smoke exposure and male gender. The mechanism of inheritance is still unclear. Familial aggregation has been described for many years. It is commonly believed that allergies are caused by multiple interacting genes, some having a protective effect and others contributing to the disease pathogenesis with each gene being influenced by the environment in a different way. Many candidate genes have been suggested in atopy and allergic diseases. The most important linkages include the genes for IL-4, IL-13, HLA-DRB, TNF, LTA, FCER1B, IL-4RA, ADAM33, TCR α/δ, PHF11, GPRA, TIM, p40, CD14, DPP10, T-bet, GATA-3, and FOXP3.[52] However, no genome wide association study has been performed specifically for allergic rhinitis. The O allele does not produce an active enzyme and has α-fucose (1 → 2) galactose disaccharides [O(H) structures] on its cell surface while in type A or B individuals, the O antigen is capped by the addition of α-*N*-acetylgalactosamine or α-galactose residues, respectively. A critical single-base deletion was found in the O gene, which results in

an entirely different, inactive protein incapable of modifying the H antigen.

Two studies found an association between blood group A and/or B antigens and atopic conditions such as rhinitis, hay fever and asthma, and the shift appeared to be largely due to a contribution from female patients with pollinosis.[53] The majority of the studies reported an association between atopic diseases such as rhinitis and the O group, while resistance was associated to A phenotype.[54] Blood group O/non-secretor subjects had lower lung function values and higher prevalence of atopy. The product of ABO and secretor genes seems also to influence the adhesion of infectious agents, thus having a modulator effect on viral and bacterial respiratory tract infection. Since the oligosaccharide composition of the cell membrane and mucosal secretions change with age and influence the adhesion of infectious agents, the age pattern of atopic diseases could reflect the interaction between cell maturation and oligosaccharide structure and its effect on susceptibility to viral and bacterial agents.

Takashi et al in 2010 found that when the total serum immunoglobulins (IgE) levels and peripheral blood eosinophil counts were widely examined to evaluate patients with various allergic diseases – asthma & allergic rhinitis coexists. However, it was found that the status of co-existence of these studies was not fully elucidated and so they did the present study. It was found out from the study that serum IgE levels were significantly higher in people with asthma with ($p<0.01$) or without rhinitis ($p<0.01$) regardless of the atopic status but not in rhinitis alone. So, conclusion was drawn that compared with rhinitis, non-antigen specific IgE production may contribute more to elevated levels of serum IgE in asthma, on top of it the significance of serum IgE & peripheral eosinophil count as indices of evaluating asthma & rhinitis might differ.

Razi E and Moosavi G A in 2010 in their study of serum total IgE levels & total eosinophil counts : relationship with treatment response in patients with acute asthma found out after analysis of the spirometry results at baseline & following 2 weeks & after treatment after dividing patients into two groups with high IgE (>100IU/L) & low IgE (<100IU/L) & comparing the FEV_1, FVC, FEF25-75%, peripheral WBC counts & eosinophil counts – that no significant differences between the groups regarding the percentage changes of the studied parameters. On the basis of these findings it was concluded that the total serum IgE, peripheral WBC count & absolute eosinophil counts cannot predict the response to the pharmacologic treatment of patients of acute asthma.

Medeiros et al in their study in 2006 concluded that in patients with respiratory allergy and increased total serum IgE levels living in areas where there is high risk of helminthic infestations – the quantification of anti Ascaris IgE can be more useful & more insightful than the parasitological stool examination.

Nelson Falsarella et al in 2011 done a test to verify if ABO phenotypes are associated with allergic rhinitis. Allergic rhinitis is a disease that affects the upper airway tract causing inflammation of the nasal mucosa. It is mediated by immunoglobulin E (IgE) antibodies which are produced after exposure to and sensitization by environmental allergens. The most common symptoms, nasal congestion, watery rhinorrhea, sneezing and itching, can be reversed spontaneously or by treatment. Allergic rhinitis depends both on environmental and genetic factors.[55] Allergic rhinitis and asthma are both respiratory diseases which have similar immunopathological mechanisms.[56] It has been suggested based on epidemiological and experimental data that allergic rhinitis and

asthma represent the manifestations of one syndrome with a wide spectrum of severity.[57] Therefore it is possible that the genetic and environmental factors causing susceptibility to asthma are also involved in susceptibility for allergic rhinitis. The ABO -blood group system is one of the genetic risk factors linked to the susceptibility to asthma in some populations. The overall frequencies of the ABO blood group phenotypes of patients and controls showed a tendency that the O blood group phenotype is associated with allergic rhinitis. Additional comparisons of the participants by gender showed a smaller number of A blood group and a larger number O blood group male compared to female patients. Based on the p-values and odds ratio, the strength of the association seems to be much higher for the O blood group suggesting that this blood group confers almost a threefold higher risk of allergic rhinitis in men than in women compared to the A blood group. The biological basis of the association between the O blood group and allergic rhinitis in men remains unclear. The *ABO* gene, responsible for the genetic control of the ABO -blood group system is autosomal and there is no evidence that its phenotypic expression and pattern of inheritance are influenced by gender.[58] However, the interaction between the O blood group and inflammatory immune response in the airway mucosa could increase the susceptibility for allergic rhinitis in men. In fact, an inflammatory immune response characterized by increased lymphocyte infiltration in the gastric mucosa was observed in O blood group patients infected by *Helicobacter pylori*.[59]Additionally, it was demonstrated that the expression of inflammatory proteins in nasal secretions is higher in men that are diagnosed with seasonal allergic rhinitis, even after treatment using anti-inflammatory drugs, compared to women.[60] Therefore, it is possible that the combined effect of the O blood group with the high expression of inflammatory proteins in the nasal secretions of male individuals contributes to the association observed in this study. In fact, the terminal structure of the glycoconjugates expressed in the O blood group differs from those expressed in the other ABO phenotypes.[61,62] Therefore, the differences between distinct glycoconjugate profiles create different binding sites on the terminal structure of the oligosaccharide chains. Since these glycoconjugates act as potential receptors for microorganisms, those expressed in the O blood group may bind allergens and influence the immune response.[63,64,65] It is possible that the profile of the glycoconjugates expressed by individuals with the O blood group, allied with the predisposition of men to express a higher level of anti-inflammatory proteins in nasal secretions favors the adherence of environmental allergens to the mucosa of the upper airway tract, thereby increasing their susceptibility for allergic rhinitis. Despite of the criteria adopted for the diagnosis of allergic rhinitis, the results of this study must be considered as preliminary as the measurement of specific IgE and the prick test were not performed for specific allergens. Even so, it sheds some light on the importance the genetic polymorphisms in the susceptibility for one specific respiratory disease the prevalence of which has been increasing over recent decades.[66]

J Singer et al found that passive immunotherapy with monoclonal antibodies is an indispensable cornerstone of clinical oncology. Notably, all FDA-approved antibodies comprise the IgG class, although numerous research articles proposed monoclonal

antibodies of the IgM, IgG, IgA and IgE classes directed specifically against tumor-associated antigens. In particular, for the IgE isotype class, several recent studies could demonstrate high tumoricidic efficacy. Therefore, this review specifically highlights the latest developments toward IgE-based immunotherapy of cancer. Possible mechanisms and safety aspects of IgE-mediated tumor cell death are discussed with special focus on the attracted immune cells. An outlook is given on how especially comparative oncology could contribute to further developments. Humans and dogs have a highly comparable IgE biology, suggesting that translational Allegro oncology studies in patients with canine cancer could have predictive value for the potential of IgE-based anticancer immunotherapy in human clinical oncology.

Susan Waserman et al researched on the IgE mediated food allergy. Food allergy is defined as an adverse immunologic response to a food protein. Food-related reactions are associated with a broad range of signs and symptoms that may involve any body system, including the skin, gastrointestinal and respiratory tracts, and cardiovascular system. Immunoglobulin E (IgE)-mediated food allergy is a leading cause of anaphylaxis and, therefore, referral to an allergist for timely and appropriate diagnosis and treatment is imperative. Diagnosis entails a careful history and diagnostic tests, such as skin prick tests, serum-specific IgE and, if indicated, an oral food challenge. Once the diagnosis of food allergy is confirmed, strict elimination of the offending food allergen from the diet is generally necessary. IgE-mediated food allergy is a leading cause of anaphylaxis, a severe, potentially fatal allergic reaction presenting to emergency departments.[67] IgE antibody responses to alpha-gal results in a delayed allergic reaction to mammalian meat, and has been associated with anaphylaxis 3–6 h after ingestion of mammalian food products (e.g., beef and pork).[68] It is the only example of IgE to a carbohydrate that has been associated with anaphylaxis. Studies strongly suggest that tick bites are the main cause of this IgE antibody response to alpha-gal, since ticks inject alpha gal through their saliva when biting humans.

Arnau Navines –Ferrer et al found out that IgE has unique properties among immunoglobulin isotypes and plays a central role in the pathophysiology of acute allergic reactions and chronic inflammatory allergic diseases. . In genetically susceptible individuals, exposure to specific allergens results in an increase of specific IgE, which can bind onto effector cells through a high affinity receptor known as FcεRI expressed in mast cells and basophils.[69] IgE is very short-lived in plasma (about 1 day), but receptor-bound IgE can remain fixed to cells in tissues for weeks or months. Moreover, IgE binding to FcεRI increases cell survival and receptor upregulation [70,71] and upon contact with a specific allergen induces the release of pharmacologically active mediators stored in the granules of mast cells (MC) and blood basophils (BS), resulting in clinical manifestations of type 1 hypersensitivity. In type 1 hypersensitivity, in the initial phase, an antigen (the allergen) is presented to antigen-specific $CD4^+$ Th2 cells, which stimulate B-cell production of IgE antibodies that are also antigen-specific. During sensitization, the IgE antibodies bind to FcεRI on the surface of tissue MC and blood BS. Later exposure to the same allergen cross-links the bound IgE on sensitized cells, resulting in degranulation and secretion of preformed pharmacologically active mediators such as histamine. All of this occurs as an immediate reaction, starting within seconds. A late reaction caused by the induced

synthesis and release of leukotrienes, chemokines, and cytokines by the activated mast cells allow the recruitment of other leukocytes, eosinophils, basophils, and Th2 lymphocytes to the site of inflammation. The allergic reaction includes symptoms like cough, bronchospasm, wheezing, diarrhea, and urticaria due to this process.[72] The use of omalizumab (OmAb), an anti-IgE drug, is approved in severe allergic asthma not controlled by conventional treatment and in chronic urticaria .[73,74] IgE is known to be involved in other pathologies, and for this reason omalizumab is currently being assessed in conditions such as allergic rhinitis, atopic dermatitis, food allergies, mastocytosis, and eosinophilic gastrointestinal disease. [75] Asthma symptoms occur paroxistically; that is, the patient is healthy for long periods although in severe cases the clinical manifestations persist. Various cells and inflammatory mediators are involved in this pathogenic process, which is conditioned partially by genetic factors. Asthma has largely been viewed as a Th2-mediated process strongly linked to atopy and eosinophilic inflammation. Early-onset allergic Th2 asthma is the most studied phenotype, accounting for 50% of subjects with asthma, and it is linked with other allergic diseases such as allergic rhinitis and atopic dermatitis. The impairment it causes ranges from mild to severe.[76] This phenotype is associated with an increase in total and specific IgE.[77] There appears to be a genetic component to early-onset asthma, as evidenced by the family history of asthma in this group.[78] In allergic asthma, the allergen can directly activate sentinel dendritic cells (DC) present in the airway epithelium.[79,80] Targeting IgE has proved to be a successful approach to IgE-related diseases with poor response to traditional treatment.

Giorgio Ciprandi in 2017 in his study stated that IgE production may be considered the hallmark of allergy, such as an indispensable factor for being allergic. He concluded that allergen sIgE could be considered a potential biomarker to individuate allergen immunotherapy (AIT) responder.

Yu Ling Tu et al in 2013 did a study on total serum IgE in Asian children in Taiwan and found out that male, atopy, allergic diseases, recent symptoms of upper respiratory infection, and lower FEV1/FVC, were associated with higher total IgE levels in univariate analyses. Multivariate analysis revealed that atopy was the single most important determinant explaining 66.1% of the variability of total IgE levels in this population. So they concluded that total serum IgE discriminates Asian children with and without atopy independent of allergic symptoms, with an optimal cut off of 77.7 kU/L. The study confirms the insufficient diagnostic accuracy of total IgE alone to detect allergic diseases, but low total IgE levels may help exclude allergic diseases.

K.M. Beeh in 2007 concluded in his study that Omalizumab is indicated for patients with baseline total IgE 30–700 IU/ mL. Once baseline serum IgE levels are obtained, there is no need to re-test IgE levels during omalizumab treatment, because total IgE levels are elevated during treatment and remain elevated. This phenomenon may appear paradoxical at first glance, but it simply reflects the fact that commercially available IgE assays also measure complexed IgE, i.e. IgE bound to omalizumab. Since these complexes have a longer half-life than free IgE, quantification of IgE after initiation of omalizumab therapy with conventional assays will result in the detection of higher IgE levels. However, it should be noted that free IgE decreases rapidly and dramatically during omalizumab treatment.

In the beginning of the 20th century, Karl Landsteiner, an Austrian scientist noted that the RBCs of some individuals were agglutinated by the serum from other individuals[81,82]. The agglutination patterns were different as noticed by Landsteiner and he concluded that blood could be divided into groups. This marked the discovery of the first blood group system, ABO.

Landsteiner explained that the reactions between the RBCs and serum were related to the presence of markers (antigens) on the membrane of the RBC's and antibodies in the serum. Agglutination occurred when the RBC antigens reacted with the antibodies in the serum. He called the antigens A and B, and depending upon which antigen the RBC expressed, blood either belonged to blood group A or blood group B. A third blood group contained RBCs that reacted as if they lacked the properties of A and B, and this group was later called "O" after the German word "Ohne", which means "without". The following year the fourth blood group, AB, was added to the ABO blood group system. These expressed both A and B antigens on the membrane of the RBC's.

In 1910, scientists proved that the RBCs antigens were inherited, and that the A and B antigens were inherited co dominantly over O. There was initially some confusion over how a person's blood type was determined, but the puzzle was solved in 1924 by Bernstein's "three allele model".

The ABO blood group antigens are encoded by one genetic locus, the ABO locus, located on chromosome 9 (9q34.1) and is called ABO glycosyltransferase, which has three alternative (allelic) forms—A, B, and O. It is therefore the combination of alleles that are inherited from parents that determines which glycoprotein (antigens) are found on person's blood cells and thereby their ABO blood type.

Structure of A, B, O antigens:

The antigens of the ABO system (*A*, *B*, and *H* determinants respectively) consist of complex carbohydrate molecules.[83] Carbohydrates are attached to glycoprotein and glycolipids on the surfaces of red blood cells. For one type of blood group, one of the three different structures, termed A, B, and O, may be present. These structures have in common an oligosaccharide foundation called the O (or sometimes H) antigen. The A and B antigens differ from the O antigen by the addition of one extra monosaccharide, either *N*-acetylgalactosamine (for A) or galactose (for B) through a α-1, 3 linkages to a galactose moiety of the O antigen. Specific glycosyltransferases add the extra monosaccharide to the O antigen. Each person inherits the gene for one glycosyltransferase of this type from each parent. The type A transferase specifically adds *N*-acetylgalactosamine, whereas the type B transferase adds galactose. These enzymes are identical in all but 4 of 354 positions. The O phenotype is the result of a mutation that leads to premature termination of translation and, hence, to the production of no active glycosyltransferase.[84]

Molecular Basis of ABO blood group:

The ABO locus encodes specific glycosyltransferases that synthesize A and B antigens on RBCs[85]. For A or B antigen synthesis to occur, a precursor called the H antigen must be present. In RBCs, the enzyme that synthesizes the H antigen is encoded by the H locus.

The H locus: The H locus is located on chromosome 19 at 19q13.3. It contains three exons that span more than 5 kb of genomic DNA, and it encodes a fucosyltransferase that produces the H antigen on RBCs.

The ABO locus: The ABO locus is located on chromosome 9 at 9q34.1-q34.2. It contains 7 exons that span more than 18 kb of genomic DNA[85]. Exon 7 is the largest and contains most of the coding sequence. Exon 6 contains the deletion that is found in most O alleles and results in a loss of enzymatic activity. The A and B alleles differ from each other by seven nucleotide substitutions, four of which translate into different amino acids in the gene product (R176G, G235S, L266M, G268A). The residues at positions 266 and 268 determine the A or B specificity of the glycosyltransferase they encode. The O allele differs from the A allele by deletion of guanine at position 261. The deletion causes a frame shift and results in translation of an almost entirely different protein that lacks enzymatic activity. There are many variant ABO alleles that encode a number of variant ABO phenotypes, but they do not encode specific antigens other than the A and B antigens.[86]

ABO blood group and Serum IgE concentrations in allergic diseases:

Obi SO et al in 2019 did a study on ABO blood group in different diseases. The apparent involvement in the pathogenesis of a significant range of human diseases, are adequately exemplified by cancers, cardiovascular [87,88,89]diseases and infections. Recent researchers have also attempted to niche out a role for ABO blood group antigens in neuroscience, implicating these [90] antigens in the development of encephalomyelitis. Despite our enormous knowledge about the complexities of ABO blood group system, its relationship with human diseases is still not completely understood; because information continues to emerge to elucidate the interplay between the blood group system and human health.

Ana lara da Costa Fereira et al in 2011 did a study to verify if ABO phenotypes are associated with allergic rhinitis. ABO phenotypes were identified in red blood cells using the haemagglutination technique. The Fisher exact and chi-square tests were employed to compare proportions. It was concluded that the O blood group phenotype is associated with allergic rhinitis in male but not in female patients.

Nur Hidayaha Dahalan et al in 2020 did a study on association of ABO blood groups with allergic diseases: a scoping review with the objective of this study was to map evidence of the association of ABO blood groups with allergic diseases such as allergic rhinitis (AR), atopic dermatitis (AD) and asthma. The majority of the studies demonstrated a significant association between ABO blood groups and allergic diseases. They found out that blood group O is prominent in patients with AR and asthma, while a non-O blood group is common in patients with AD. This scoping review serves as preliminary evidence for the association of ABO blood groups with allergic diseases. Further studies need to be conducted so that the relationship between ABO blood groups and allergic diseases can be fully established. This could be helpful for clinicians and health professionals in consulting and managing patients who suffer from allergic diseases in the future.

F Ronchetti et al studied, ABO/Secretor genetic complex and susceptibility to asthma in childhood and a positive association has recently been reported in adult subjects between O/non secretor phenotype and asthma. The proportion of O/non secretor in asthmatic children was

higher than in controls, thus confirming the association found in adults. The association was more marked in males than in females. In males, the pattern of association between the joint ABO/Secretor phenotype and asthma is dependent on the age at on-set of symptoms. Since the oligosaccharide composition of cell membrane and mucosal secretions is controlled by the cooperative interaction of ABO and Secretor genes, and since such composition influences the adhesion of infectious agents, the age pattern could reflect a more general interaction between developmental maturation and oligosaccharide structure concerning their effects on susceptibility to viral and bacterial agents.

Thais Amarante Peres de Paula Couto et al in 2014 did a study of the total IgE plasma levels vary according to gender and age in Brazilian patients with allergic rhinitis and concluded that total IgE plasma levels are higher in young adult males than in females suffering from allergic rhinitis. Evaluating total IgE plasma levels can be useful to identify patients at risk of allergic rhinitis in areas with low industrial pollution.

Mohandas et al in 2005 in ABO genetics found that the ABO gene locus is on chromosome 9. At its most basic A, B, O- these 3 allelic options are available in which A& B are codominantly expressed & O is apomorphic & the gene product is an Enzyme A or B transferase – which requires the presence of H antigen in order to act. This means – the ABO genetic pathway is also dependent on the of the H gene of the H blood group system. The H blood group system is separate & independent from the ABO system residing on chromosome 19. The H antigen is high prevalence occurring at a frequency of 99.9% in all populations & concluded that ABO blood group has been shown to be of high clinical relevance in transfusion medicine – this contributes to transfusion reactions that are highly dangerous – when presented due to incompatibility & haemolytic disease of the new born. There is a strong link between ABO blood group & susceptibility to diseases – individuals with a particular ABO blood group are more predisposed to certain diseases more than persons with other ABO blood group. Thus, the clinical significance of the ABO blood group system extends beyond transfusion medicine & several reports have suggested an important involvement in the development of cardiovascular, oncological & other diseases.

Emmanuel Ifeyanyi et al in 2019 published an update on susceptibility of individuals to disease based on ABO blood groups. The ABO blood group system is reported as the most clinically significant of all the blood group systems. This is because of the vast majority of population carrying pre formed ABO antibodies; this is the only blood group system where if you lack the antigen you will make the corresponding antibody without deliberate immunization. However, more studies particularly in areas of genomics- are needed to completely unmask the molecular mechanisms linking ABO blood group system & the statistical association document for some disease conditions. If that is achieved – blood group antigen typing may become a veritable tool in human disease monitoring or diagnosis.

Giancarlo Maria Liumbrunoet al in 2013 The antigens of the ABO blood group system (A, B & H determinants, respectively) are complex carbohydrate molecules on the extracellular membranes of RBC membranes.[1] However, alongwith their expressions on RBC's, ABO antigens are highly expressed on the surface of a variety of human cells & tissues including the epithelium, sensory neurons, platelets & vascular

endothelium 2. So it was concluded that despite our enormous knowledge about the complexities of the ABO blood group system- its relationship with human diseases is still not completely understood as information continues to emerge to elucidate the interplay between the blood group system & human health.

Massimo Franchini et al in 2015 did a study on the evolutionary aspects of ABO blood groups in humans. In this review, after succinct description of the current knowledge on the association between ABO blood groups and the most severe diseases, it was aimed to elucidate the particularly intriguing issue of the possible role of ABO system in successful aging.

Brachtel R et al did a study on the associations between atopic diseases & the polymorphic systems ABO & red cell acid phosphatase- they found that blood group O could be demonstrated in patients who have both arthritis and asthma from previous studies- so the limitation of the study was that it was essentially retrospective in nature – so a valid conclusion cannot be safely made on this relationship based on this study Methodology. On the other hand, a cross sectional study in Germany showed that persons who had atopic conditions like atopic dermatitis, hay fever, allergic rhinitis, asthma, acute urticaria –showed the incidence of blood group antigens A and B was higher- in these patients than in control group, whereas patients with both diabetes & asthma presented more with group A phenotype. Moreover, blood group B was associated with greater severity of chronic inflammatory pulmonary diseases – as well as with asthma from chronic lung infection. So, the conclusion was that although reports consistently show a relationship between ABO histo blood groups with venous / arterial thrombosis & gastric/ pancreatic malignancies – there is no unanimity in the findings regarding the association of ABO &other histo blood groups with risk of respiratory atopy. Nonetheless, much of the evidence from various studies indicates that the association with respiratory atopy risk remains significant. Further research using systematic reviews with meta analyses & case control studies with large sample sizes are recommended to validate the emerging evidence on this relationship – which may in future support the use of blood group typing in evaluating respiratory atopy risk in children.

Rasha Saadi Abbas et al 2020 studied the relationship between asthma severity & ABO blood group phenotype in sample of Iraqi patients with chronic bronchial asthma- to find out the ABO blood group distribution among asthmatic patients – in addition to the association between blood group phenotype & asthma severity where ABO & Rh blood group were determined using agglutination reaction method. Asthma Control Test (ACT) & pulmonary function test (PFT)using spirometry – were used for determination of asthma severity. The blood group distribution among asthmatic patients were of the order of B>A>O>AB with frequency distribution of 33.33%, 30%, 28.33%& 8.34% respectively with significant differences amongst them($p<0.5$) & 90% of patients were Rh positive. As regards asthma control test (ACT)- 78.3% presented with uncontrolled asthma- of which 25% were of blood group O, followed by blood group A, B & some patients had severe asthma mostly in patients with blood group A (23.4%) & O (21.7%). Severe asthma in case of forced vital capacity ($FVC<60$) is mostly found in patients with blood group O (20%). Blood group B (26.7%)is

associated with severe asthma in case of peak expiratory flow (PEF<60).

Boris Jelavic et al in 2018 did a study on the topic of ABO & Rh D blood groups in nasal polyposis and found out that there were no significant differences between patients & controls in the distribution of A, AB, O & B alongwith Rh D phenotypes and concluded that ABO & Rh blood group systems are not associated with the development of nasal polyposis.

Nallur Ramachandra et al in Indian perspective found out by their study that there is lack of association between asthma & ABO blood group.

In one study being done for association of blood group and incidence of asthma & COPD- it was found that the most frequent blood group was A and least AB group & the distribution of individual blood types in asthma – was not different from that in COPD patients. However, significant differences were found between the distribution of O & pooled non-O blood types (A, B & AB). The pooled category was more frequent in asthma & COPD both. The association was more marked in males than females. In males the pattern of association between the joint ABO/ secretor phenotype & asthma is dependent on the age at onset of symptoms. Since the oligosaccharide composition of cell membrane & mucosal secretions is controlled by the cooperative interaction of the ABO & secretor genes – since such composition influences the adhesion of infectious agents. The age pattern could reflect – a more general interaction between the developmental maturation & oligosaccharide structures concerning their effects on susceptibility to viral & bacterial agents.

M.P Villa et al did a study on the ABO/ Secretor genetic complex & susceptibility to asthma in childhood. The secretor gene FTU-2 that encodes for a 2-α-L fucosyltransferases & the ABO blood grouping system that encodes for glycosyltransferases act in concert to build up oligosaccharide structure in exocrine secretion systems including respiratory tract. [91,92, 93] Specific oligosaccharide epitopes are necessary for recognition of microorganisms.[94] The product of ABO & secretor genes seem to influence the adhesion of infectious agents- thus having a modulatory effect on viral & bacterial respiratory infection.[95] A combined analysis of the ABO blood groups & salivary secretor phenotypes- was recently performed in cohort of coal miners. Lower lung function & higher prevalence of wheezing & asthma in non-secretor subjects of blood group O was shown. Glycosyl transferases are controlled by the ABO system & are very helpful in building oligosaccharide structures on the cell surface – of erythrocytes & so it was concluded that – blood type is not a prognosting differentiating between the occurrence of asthma or COPD patients – although both are less common in people with blood type O.

The hyperimmunoglobulin E syndrome (HIES) is a complex & rare primary immunodeficiency disorder characterized by recurrent skin & lung infections, dermatitis & elevated serum IgE concentrations.[96,97,98] This disease was initially called Job's disease by Davis & colleagues. In 1972, Buckley redefined the syndrome – as he found extremely high levels of serum IgE in patients suffering from the syndrome. Other manifestations of the disease came into limelight like skeletal, connective tissue, cardiac & brain abnormalities. [99,100,101] Two forms of HIES was recognized – dominant (classical) & recessive.

Brief history of Eosinophils: Eosinophils are granulocytic white blood cells[102]. Recognized by Paul Ehrlich about 135 years ago.[103] Eosinophils are components of immune system associated with allergy of various types. These cells are acid loving granules stain with acidic stains. They are also called acidophils. Granules stain brick red by Leishman's stain. Granules contain chemical mediators like histamine and proteins like peroxidase, ribonuclease, deoxyribonuclease, lipase, MBP.

In 1673, Leeuwenhoek found some structures in the blood which he called as small round globules and attributed colour of blood to these granules. Later on Swammerdam observed the RBC's and named them ruddy globules. Since then various works have been done in the field of hematology and various investigations have evolved out by the works of different scientists. As mentioned before, eosinophil was discovered by Paul Ehrlich as a special type of granulocyte in 1879. Its large refractile granules aroused such interest that by 1914 Schwartz was able to write a review which included many references.

In 1967, Lowel reported that measurement of total eosinophils in blood was helpful in the evolution of asthmatics. In 1972, *Hosinger et al* presented the preliminary observation that improvement in pulmonary function coincided with a decrease in eosinophil count. Eosinophilia has been found in patients with exfoliative dermatitis, psoriasis, pruritus, prurigo, eczema, dermatitis venereta, icthyosis, mycosis fungoides, pityriasis rubra, facial granulomas & scabies. [104,105,106,107]

Morphology of Eosinophil: Mature eosinophil has a diameter of 10-14 micrometer in blood films & because of their large, bright red staining coarse granules are easily recognized in blood films or secretions of tissues.[108] The nucleus usually has two lobes, although three or more lobes are observed. Cytoplasmic granules are coarse & highly refractile eosinophilic (orange red) under Leishman's stain. On electron microscopy, the amount of euchromatin is more abundant than in mature eosinophils in keeping with the eosinophil ability to engage in major biosynthetic process. The granules of mature eosinophils are ovoid, membrane bound organelles 0.15 to 1.5 µm in length & 0.1-0.3µm in width. Human eosinophil granules has a central electron opaque core or crystalloid which is surrounded by a less dense matrix. The crystalloid contains basic proteins which are rich in arginine & lysine. They also contain phospholipids & probably melanin. [109,110,111]

Origin & development: Eosinophils are developed in the marrow, where they can be distinguished from neutrophils at the promyelocyte of development. In the peripheral blood, only mature eosinophil & occasional band forms may be seen in normal person. In addition, eosinophilic promyelocyte contain a few large granules which stain by Romanowsky stains. This appears to be lost by attrition as a consequence of subsequent mitotic divisions

Structural and functional characteristics of Eosinophils: [112]

Features: The granules of eosinophils contain following major chemicals[113-121] which are major basic protein, eosinophil cationic protein, eosinophil derived peroxidase, eosinophil derived neurotoxin, cytokines, other chemicals.

Major basic protein (MBP) is a major toxic product of eosinophil. It is toxic against many intestinal parasites & their larvae eg, ascaris, schistosoma etc.

MBP is also toxic to pneumocyte & epithelial cells of respiratory tract. MBP also makes the bronchial tree hyperresponsive to bronchoconstrictors.
Eosinophil cationic protein (ECP) is high in arginine. ECP is toxic to helminthic parasites and tracheal epithelium. ECP produces neurotoxicity.
Eosinophil peroxidase (EP)is a haem containing protein. It has 68% homology with neutrophils myeloperoxidase & other peroxidases. EP is toxic to the parasites & pulmonary tissue. Eosinophil derived neurotoxin (EDN) is a glycosylated protein having striking ribonuclease activity. EDN is also secreted by mononuclear cells. It is toxic to the neural tissue. [122,123,124,125]

Cytokines are synthesized outside the granules but stored in granules. The important cytokines secreted from eosinophils are: interleukins, macrophage inhibiting factor (MIF), transforming growth factor, tumor necrosis factor. TGF-α mediates the important role of eosinophil in wound healing. Many of the cytokines like interleukins like IL-5, IL-3, and GM-CSF act in autocrine fashion as eosinophil growth factor. MIF plays a role in the genesis of adult respiratory distress syndrome. [126,127, 128,129]

Functions: Eosinophil plays an important role in the host defense mechanism. Eosinophil participates in two important defense mechanisms of the body.

-Against helminthic infections
- Against allergy
- Eosinophils also has a role in immunity

In allergic conditions like bronchial asthma, eosinophil plays a major role in pathogenesis. Bronchial hyperreactivity is correlated with eosinophilia & airway eosinophil content. Inhibition of airway eosinophilia by steroids has been reported to cause improvement in bronchial hyperresponsiveness & asthmatic symptoms. Although steroids cause eosinophilia by eosinophil apoptosis, the main mechanism is the inhibition of production of IL-5 and IL-3from type 2 helper cells. It is not clear whether eosinophil prevents allergy & therefore eosinophilia occurs in allergy or eosinophilia in allergy aggravate the situation. However, the recruitment of eosinophil at the site of allergic inflammation is accompanied by an increase in number of activated T-cells & monocytes. It has been hypothesized that asthma is an eosinophil mediated disease driven by type 2 helper lymphocytes that secrete IL-5 & IL-3[130, 131,132,133]

Mediators are released by degranulation following activation of eosinophils & are toxic to both parasites & host tissues. Eosinophils make up 1-7% of WBC's in circulating blood. Eosinophils are also found sparsely in tissues like – medulla of thymus, lower GIT, ovary, uterus, spleen, lymph node & are not seen normally in lungs, skin, esophagus, other internal organs & presence of eosinophil in them implies some disease state. When eosinophils act as proinflammatory leucocytes – adverse tissue reactions occur mainly due to production of large number of cytokines & chemical mediators. So detection of eosinophilia becomes more important to prevent organ damage by these inflammatory substances – in whom the clinical manifestations depend upon the site of eosinophilic infiltration – leading to the extent of damage done .

Eosinophils also possess a risk for anesthesia-as when the number of eosinophils are increased – it increases the risk of bronchoconstriction due to histamine & other mediators. After research it was found that, surgeries were delayed as a result of increased blood eosinophilia – an

increase in number of such delays – prompted the undertaking of such study - in order to check the prevalence of eosinophilia in this geographic region.

AEC was done by a standard method using the WBC pipette, diluting fluid and haemocytometer slide with improved Neubauer counting chamber.[134] Normal value: 40-440 cells/cubic mm of blood. A sample with a AEC higher than 440 cells/ cu.mm of blood was considered to be significant.[5] Blood eosinophilia was categorized as: Mild- when AEC is between 440-1500cells/ cu.mm of blood. Moderate- when count is between 1500-5000 cells/cu.mm of blood. Severe- when AEC is >5000cells/cu.mm of blood. Tissue Eosinophilia: It is mostly diagnosed by clinical presentation & on laboratory findings – both gross & microscopic with histopathology pointes towards diagnosis of tissue eosinophilia.

Absolute eosinophil count & ABO blood group :

William R Best et al in 2019 studied the variation & error in eosinophil counts of blood & bone marrow and stated that – recent interest in changing levels of circulating eosinophils – as an index of 11 oxysteroid output from the adrenal cortex- which demands a critical evaluation of the accuracy of individual counts of the validity of comparing successive counts & of physiologic variations in eosinophil level, lymphatic filariasis, ovarian cancer, parasitic infestation , primary immunodeficiency, trichinosis, ulcerative colitis . Parasitic diseases & allergic reactions are to medications are among the more common causes of eosinophilia. Hypereosinophilia that causes organ damage are called as hypereosinophilic syndrome –this syndrome tends to have an unknown cause or results from certain types of cancer such as bone marrow or lymph node cancer. Specific diseases & conditions that can result in blood or tissue eosinophilia include AML, ascariasis, asthma, atopic dermatitis, cancers, chrug-strauss syndrome, crohn's disease, drug allergy, eosinophilic esophagitis, eosinophilic leukemia, hay fever, Hodgkin's lymphoma, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome – in which there is an extremely high eosinophil count of unknown origin. Eosinophilia occurs – when a large number of eosinophils are recruited to a specific site in the body or when bone marrow produces too many eosinophils.

Regulating Inflammation: Eosinophils help promote inflammation – which plays a beneficial role in isolating & controlling a disease site. But sometimes, inflammation maybe more- than is necessary leading to troublesome symptoms or even tissue damage. Il-5 is a relatively specific cytokine for the eosinophil lineage & is responsible for selective growth & differentiation of eosinophils. In collaboration with IL-5, the eotaxin chemokines induces eosinophil trafficking & accumulation by promoting chemoattraction. There is a midmorning drop of 20% from the 8AM level – with a return to that level – shortly after noon & a rise of approximately 30%above it in the middle of the night, slight dips appear to follow meals. Fasting subjects shows a continuous fall – extending into the early afternoon. Normal individuals maintain within broad limits – the same general level eosinophils – over prolonged periods This does not appear to be altered by menstruation, minor colds or season of the year.

Interpretation of induced changes of circulating eosinophils: The maximal eosinopenia from ACTH or cortisone – occurs at about 4 hours. Eosinopenia of 50% or more- 4 hours after S/C or IV administration of Epinephrine (0.2 mg or more) –would seem to imply adequate function

of the hypothalamic – pituitary – adrenal chain. Failure to obtain adequate response may be due to chance & physiologic variation. Refractoriness to a single dose of ACTH, epinephrine or ephedrine. Failure of response to single dose of ACTH has also observed in conditions other than Addison's disease. The reason for this failure is not always apparent. The individual might be tested while subjected to stimuli inherent to his disease or his environment which are known to cause a release of adrenocortical hormones. The relatively slight additional stimulation of the test may then be insufficient to induce further eosinopenia, a phenomenon which we have observed while testing patients under stress & in acute illness.

Behdav Navabi et al in 2016 studied the primary immunodeficiencies associated with eosinophilia found that eosinophilia is not an uncommon clinical finding – however, diagnosis of its cause can be a dilemma once common culprits namely infection, allergy & reactive causes are excluded. Primary immunodeficiency disorders (PID) are known differentials of eosinophilia. However, the list of PID's typically reported with eosinophilia is small & the literature lacks an inclusive list of PID's which have been reported with eosinophilia. This motivated the researchers to review the literature of all PID's which have been described to have elevated eosinophils – as this may contribute to an earlier diagnosis of PID & further standing of eosinophilia & concluded that the list of PID's is extensive – which have been reported with eosinophilia as these list help clinicians to consider an extended differential diagnoses when tasked with exclusion of PID as a cause of eosinophilia. The limitations were that the true frequency of eosinophilia in individuals with PID conditions is subject to reporting omissions & biases. The AEC is not described for every PID & therefore the degree & the range of eosinophilia – is derived from a low number of cases. The degree of eosinophilia can be markedly varied in each PID. Given the variability of the degree of eosinophilia – this is unlikely to be of major diagnostic assistance – but severe eosinophilia is less common & have more diagnostic utility. So it was concluded that there are more primary immunodeficiency than typically recognized & eosinophilia has been reported with many primary immunodeficiencies.

Tjeerat et al showed that elevated eosinophil counts were associated with male gender and with an urban population.[135] and they found that there was no gender preponderance & eosinophilia was dominant in rural population with no particular reason attributed for an increase in eosinophils in rural population.

Makkar et al showed that 70% of patients with vague symptoms & 52% were having mild eosinophilia. Eosinophilia maybe observed in body fluids – as well as body tissues & when the latter becomes obvious called tissue eosinophilia (>20 eosinophils/high power field)

Falconieri et al found 13 cases of squamous cell carcinoma of oral cavity- characterized by prominent eosinophilic infiltration of the stroma.[136] Tumor associated tissue eosinophilia has been observed in diverse sites including head & neck region. Studies have shown that tumor associated tissue eosinophilia has a favorable prognosis – suggesting that eosinophils play a protective role against epithelial tumors. [137,138,139,140]

Nathan D Montgomery et al in 2013 studied diagnostic complexities of eosinophilia & concluded that eosinophilia is a haematologic abnormality with diverse etiologies and the

underlying cause can be divided into reactive, clonal & idiopathic. Reactive eosinophilias can be triggered by allergy, infection, various medical conditions, neoplasms. Most eosinophilias are reactive – polyclonal processes. In all these reactive processes – the increase in AEC appears to be mediated by cytokines principally IL-5- which promotes proliferation of eosinophils & their precursors.[141] Clonal eosinophilia are eosinophilias associated with myeloid leukemias

Marc E Rothenberg et al in 2006 studied and found that eosinophils have been considered end stage cells involved in host protection against parasites, however, nowadays, eosinophils are found to be pleiotropic multifunctional leucocytes involved in initiation & propagation of diverse inflammatory responses as well as modulators for innate & adaptive immunity. Eosinophils have been found to have a role in homeostatic mechanism including developmental biology & innate & adaptive immunity.

Ioanna Tsiligianni et al in 2018 stated that in patients with or without asthma – it is important to recognize two broad groups of patients with blood eosinophil counts of less than 600 & those with a high eosinophil count should be looked differently. Elevation of sputum eosinophils has shown predictability as a marker of ICS response – which has led to the interest – in using blood eosinophil as a surrogate measurement.

Negewo *et al* has showed that blood eosinophils can help identify the presence or absence of sputum eosinophils.[142] Sputum eosinophil count >3% is observed in upto 28% of cases with acute exacerbations.[143] The studies by Negewo et al & Bafadhel study showed a eosinophil count of more than 2% in blood served as biomarker of eosinophil count of >3% in sputum & 40% of patients showed a discordance between sputum & blood at the blood eosinophil cut off point of $0.3x10^9$/Litre. Therefore, there remains significant doubt as to whether blood eosinophils actually depict tissue & sputum eosinophils. Copenhagen lung study, was recently reviewed & the results showed an increase in exacerbations when blood eosinophil count was above 0.34[144]

A meta-analysis by Ho et al – which included 14 observational & randomized control trials with parallel groups – comparing COPD patients with an elevated blood eosinophil count defined as having more than 2% eosinophils – either in the blood or sputum – revealed a similar risk of both exacerbations at 12 months & in the hospital mortality with or without elevated blood eosinophil.

A recent study by Casanova et al using data from CHAIN & BODE cohort showed that exacerbation rates did not differ in patients with & without eosinophil counts above 300cells/μL[145] consistent with the ECLIPSE study[146]

Zysmann et al reported that for all cut offs, 2% versus <2%, ≥3% versus <3% &≥4% versus <4% - there was no difference between eosinophil positivity & eosinophil negative groups in exacerbation rate , history of asthma or 3 year survival.[147] Eosinophils are not stable throughout the life of a patient with COPD[148,149]- and it has been reported that blood eosinophil counts vary within the same person at different times of the day & on different days even in healthy subjects[150] This lack of stability could result in blood eosinophil not being a reliable biomarker.

Myeong Heon shin et al in 2009, studied the eosinophil mediated tissue inflammation responses in helminth infection and found that eosinophilic leucocytes function in host protection against parasitic worms – in turn, helminthic parasites harbor specific molecules to evade or paralyze eosinophil associated host immune responses – this molecule facilitate the migration & survival of parasitic helminths in vivo. These competitions between eosinophil & worm leads to formation of stable equilibrium state between them. Recently, it has been found that eosinophils can function as antigen presenting cells (APC's) –eosinophils can process & present a variety of microbial, viral, parasitic agents[6]*Mawhorter S.D. et al* identified surface molecules that are associated with physiologic activation of eosinophils by applying whole blood flow cytometry to eosinophils. The granulocyte activation marker CD66was also upregulated on eosinophil from helminth infested patients, conversely, in vivo CD23 expression on eosinophils was decreased in the presence of parasitic infection. Expression of the eosinophil surface molecules CD69, CD81& CD 23 was significantly enhanced after cytokine stimulation in vitro with IL-3 or GM-CSF.

The present study was undertaken with the aim to measure and find any correlation between serum IgE and absolute eosinophil count among ABO blood group individuals and among gender. A total of 234 young healthy individuals were randomly selected for the study.

The purpose of the study was to establish association between serum IgE & absolute eosinophil count among ABO blood group in young healthy adults as a marker for the development of allergic disorders like allergic rhinitis, atopic dermatitis & asthma & to find out the hypersensitivity to particular allergen among gender alongwith the development of pulmonary complications. Also, to find out which blood group among the ABO blood group types is more prone to development of allergic disorders.

The values of serum IgE & absolute eosinophil count points towards positive correlation of these values (ie, higher values) points towards more chances of ABO blood groups having the chances of having allergic diseases in the future- however, the mechanisms by which blood type can affect the development of allergic diseases remains unknown.

In this study, several important insights were gained. First, in the study, participants with blood group B were found to be more susceptible than those with other groups to allergic diseases in this part of India in getting diseases of allergic nature like allergic rhinitis & asthma.

Gangopadhayay et al found that the blood group B was most prominent type in patients with atopic dermatitis followed by blood group A & this finding was consistent with the results reported by Abid[151] & Brachtel[152]et al. These results suggest that certain ABO blood groups have been established as a risk factor for developing allergic diseases in the future.

Secondly, by studying the history & family preponderance of the cases, it is found out that in young healthy adults of Gauhati Medical College & Hospital who are exposed to environmental allergens & have a genetic preponderance can develop allergic diseases like atopic dermatitis, allergic rhinitis & bronchial asthma. In fact, out of the allergic diseases bronchial asthma is such that it can lead to a substantial loss of the productive years in the life of a person and even cause mortality & is recognised as a serious global health problem. So, values obtained by doing serum IgE and absolute eosinophil count is a triggering factor for the onset of allergic diseases, if the values are more than normal. Overall, the values of serum IgE & absolute eosinophil count establishing a relationship with ABO blood groups produced significant outcome after the unwanted values were eliminated.

Thirdly, evidence was established between increasing values of serum IgE & absolute eosinophil count, however no gender predominance could be established. No gap was highlighted in geographic association between values of serum IgE, absolute eosinophil count with ABO blood groups.

As we have found in our study that serum IgE and absolute eosinophil count were significant ($p<0.05$) among blood groups and within them B blood group people has significantly increased serum IgE levels as well as absolute eosinophil count. Those individuals with blood group B & with genetic predisposition called atopics might have a personal tendency to develop IgE – when exposed to otherwise harmless environmental allergens because most probably such individuals have a allergen specific IgE(sIgE) probably in their serum reflecting their exposure to allergens. It may be so pertinent that persons of B group living in tropical countries like India where there is helminth endemic, in them serum IgE are increased several folds compared to atopic people in developed countries indicating that helminths are capable of inducing IgE synthesis markedly. Lynch et al also reported that helminths enhance polyclonal synthesis of IgE resulting in high total IgE (tIgE) levels –while downregulating the production of sIgE. The mechanism of immune evasion by helminths is not well elucidated till date. So more studies involving different genetic loci for the forms of IgE needs to be further dealt.

In our study some subjects were found to be suffering from psoriasis ~particularly palmo-plantar psoriasis and incidentally they were also found to be having both serum IgE and absolute eosinophil count raised which exemplifies the observation of Paparo SB et al who observed that allergic diseases & psoriasis with high levels of serum IgE as both these diseases are characterized by an immunological disorder – involving cytokines & other inflammatory mediators with massive activation of CMI.

In our study it was observed that the serum IgE as well as absolute eosinophil count was significantly increased (p value<0.05) among non O blood groups signifying that healthy young adults of Gauhati Medical College are more prone to development of allergic manifestations, diseases as well as pulmonary complications whereas Clara Carpegianni et al found that there was predominance of O blood group in the development of allergic rhinitis, whereas other two studies have found an association between blood group A and or B antigens & atopic conditions such as rhinitis, hay fever, asthma.

In the current study, it was observed that there was a strong positive correlation between serum IgE and absolute eosinophil count in male & female with no gender predominance in the development of allergic manifestations whereas study by Nelson Falsarella et al showed additional comparisons of the participants by gender showed that a smaller number of A blood group and a larger number of O blood group male have more propensity to develop allergic symptoms compared to female patients. The biological basis of the association between the O blood group & the allergic rhinitis in men remains unclear. The ABO gene responsible for the genetic control of the ABO blood group system is autosomal & there is no evidence that its phenotypic expression & pattern of inheritance are influenced by gender. In fact, the terminal structure of the glycoconjugates expressed in the O blood group differs from those expressed in the other ABO phenotypes.

In my study it was also observed that there was a negative correlation between serum IgE and absolute eosinophil count in O blood group which is non-significant

($p>0.05$) though. In non O blood group a significant positive correlation ($p< 0.05$) was seen ie, as the serum IgE level increased there was a significant increase of the absolute eosinophil count in non O blood group. It was observed by Nur H Dahalan et al that blood group O is prominent in patients with AR & asthma while non O blood group is common in patients with atopic dermatitis. This scoping review serves as a preliminary evidence for the association of ABO blood groups with allergic diseases. It has not been strongly established & needs further evaluation for it could be helpful for clinicians & health professionals in consulting & managing patients who are likely to suffer from allergic diseases in the future. So the implications & findings from my study would serve as a word of caution for those subjects who have high values of serum IgE and absolute eosinophil count alongwith those of blood group B to be proactively exert a cautious approach and avoid the possible allergens which may trigger a vicious allergic reaction and subsequently lead to the development of complications which serves the main objective of this study to identify young healthy adults prone to allergic diseases and ensure better preventive and therapeutic modalities for them.

In my study it also came to the forefront that there was a positive correlation between serum IgE & absolute eosinophil count among individuals of age group between ≤20, 21-30, 31-35 years respectively. Moreover, a significant positive correlation ($p<0.01$) was seen among all three age distribution groups of ≤20, 21-30, 31-35 years ie as the serum IgE increased there was a significant increase of absolute eosinophil count among these groups which contradicts the study done by Thais Amarante Peres de Paulo Couto et al which was a study done in a Brazil in which serum IgE plasma levels vary according to gender & age with the conclusion that serum IgE plasma levels are higher in young adult males than in females suffering from allergic rhinitis.

In this study among the ABO blood group B> A> AB>O on the basis of blood group B & A with positive correlation with serum IgE and absolute eosinophil count & negative correlation for AB & O blood groups. Similar study was done by Rasha S Abbas with respect of asthma severity & ABO blood group. The blood group distribution among asthmatic patients was of the order of B>A>O>AB with frequency distribution of 33.33%, 30%, 28.33% & 8.34% respectively with significant differences amongst them ($p<0.05$)

In this study there was no significance in respect of gender with the values of serum IgE and absolute eosinophil count showing no significance ($p>0.05$). In the study by Tjeerat et al which showed that elevated eosinophil count was associated with male gender & with urban population and they found that there was no gender preponderance but eosinophilia was dominant in rural population with no particular reason attributed for an increase in eosinophils in rural population.

CONCLUSION

The present study was undertaken with the aim to analyze the serum IgE levels and absolute eosinophil count among the different ABO blood groups of Gauhati Medical College and Hospital and to find a relationship between the two parameters amongst the blood groups. Our secondary objective directed us to find the correlation between serum IgE and absolute eosinophil counts among gender.

Our study showed a significant statistical difference between serum IgE and absolute eosinophil count among the blood groups in young healthy adults but the results of statistical analysis were insignificant with respect to gender. As observed from the study the mean serum IgE in B blood group individually and as a whole in non O blood group was significantly the highest. However, the mean of the absolute eosinophil counts significantly increased in case of B blood group. The mean serum IgE levels had no effect with increasing age among young adults. Our study showed a slight positive correlation between serum IgE and absolute eosinophil count among B and A blood group respectively and also showed no significant correlation among the gender.

The above findings demonstrate that an increased serum IgE level is probably associated with an increase in the eosinophil count and that ABO blood group influences the changes in serum IgE levels. As it is an established fact that increased serum IgE levels are associated with increased incidences of allergic and hypersensitive disorders and also with an increased risk of developing pulmonary complications in later life, increased serum IgE levels may become an important parameter to be recognized as a risk factor in the development of the pulmonary complications in later periods and its measurement along with the knowledge of its association to the blood group may possibly predict the development of an initial hypersensitive reaction and also help in evaluating its prognosis taking in consideration the traditional risk factors associated with it.

There are more allergic disorders than typically recognized. Eosinophilia has been reported with many primary immunodeficiencies including severe combined, combined humoral, phagocytic & innate immunodeficiencies. Based on AEC values in the tests & those from the literature reveals that – eosinophilia can be driven by varied processes including imbalances in Th1/ Th2, cytokine derangements, infections & medications.

However, the study encountered some limitations- As it was a time bound study of one year our sample size was small (n=234). Confounding factors such as ethnicity, nutritional status, geographical location etc. have to be adjusted for statistical procedures to find out the changes in the variables independent of these factors. Follow up of the subjects be done to ascertain the effects of the increased serum IgE levels & increased AEC values. Determining the true frequency of eosinophilia in individual primary immunodeficiency (PID) conditions – is subject to reporting omissions & biases. The AEC is not described for every case of disease & therefore the degree & range of eosinophilia –is derived from a low number of cases. The degree of eosinophilia can be markedly varied in each type of allergic disorders. Given the variability of the degree of eosinophilia – this is unlikely to be of major diagnostic assistance, but severe eosinophilia is less common & have more diagnostic utility. The quality appraisal assessment was excluded – thus the readings of some values maybe not up to the mark. The population representation does not represent the entire Gauhati Medical College & Hospital although I have tried to mitigate it as much as possible by selecting the cases from different corners of the city who have come under the ambit of the study. The ongoing Covid-19 pandemic also lessened the constructive time frame of the study.

Recommendation and Future scope: Prospective studies with a larger sample size and proper follow up should be done to further establish more firmly the relationship of levels of IgE and absolute eosinophil count with respect to development of allergic & primary immunodeficiency disorders thereby generalizing the conclusion from our study. Newer techniques of serum IgE estimation and treatment of hyper IgE disorders directed at targeted population may be helpful for the treatment and the prevention at early stages of the development of allergic disorders and their complications which may affect severely the productive time period of ones lives, more so in case of young adults. Studies demonstrating linkages of serum IgE levels with other risk factors of pulmonary & connective tissue and immune mediated disorders should be done to have an in-depth knowledge of the mechanism involved with the disease for benefit in both preventive & therapeutic aspects. Researchers should asses the rural-urban, male-female, geographical locations, & on proinflammatory markers of allergy in the future.

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