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INTERPRETATION OF BLOOD CULTURE AND SENSITIVITY IN THE FEBRILE THALASSEMIC PATIENT IN THE PAEDIATRICS AGE GROUP

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ABSTRACT

Across sectional study done in the thalassemic care centre in Najaf governorate from the 1st of February to the 1st of July 2009 to identify the most causative microorganism for bacteremia thalassemic patient and sensitivity of these organisms to antibiotics. Seventy patients included in the study age range from (4 months- 12 years) M: F ration 2:1those with positive blood culture was 10%. The study concluded that bacteremia in thalassemic patient correlated with splenectomy. So we need regular use of antibiotics and vaccination after splenectomy because the splenectomized patient is immunocompromised and are more liable for bacteremia. Early detection of sign and symptoms of bacteremia prevent complication.

***Keywords**:* - blood culture, febrile thalassemic, paediatrics age group

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INTRODUCTION

Thalassemia is the most common genetic disorder globally characterized by decreased production of haemoglobin, which leads to anaemia (1). Genetic of haemoglobin synthesis:- Hemoglobin synthesis is directed by controlling genes that are switched on and off at certain stages of human life, resulting in different globin chain synthesis at different ages (2). The genes controlling the alpha-globin chain are located on chromosome 16, while the beta chain genes are located in chromosome 3 (3). Beta chain production starts at about the 9th gestational week; then haemoglobin A becomes detectable (1). Fetal haemoglobin synthesis declines but persists until 9 months of age, at which time the switch is complete. Normal A2 level is 1 to 3 %, the impotence of hemoglobin A2 is that it is diagnostically elevated in the beta thalassemias carriers. To summarize, normal hemoglobin A =96%, hemoglobin F 1% and hemoglobin A2 3%. Risk factors include a family history of thalassemia and ethnic background susceptible to the disease. The incidence varies widely throughout the world.

The inheritance of a defective gene causes an imbalance in the alpha and beta proteins globin chains necessary for haemoglobin production. There are two types, alpha and beta-thalassemia. Genes must be inherited from both parents to acquire the disease; if one gene is inherited; the person will be a carrier of the disease but will not have symptoms; alpha thalassemias occur in people from South East Asia and China and are caused by deletion of a gene or genes from the globin chain. The most severe form of alpha thalassemia loss of all four alpha-globin genes is incompatible with life. The fetus is stillborn or critically ill with hydrops fetalis. Deletion or mutation of three alpha globin genes results in HbFI disease, characterized by splenomegaly, modernly severe chronic hemolytic anaemia, one of two of the four alpha-globin genes may have only mild microcytosis or mild hyperchromic anaemia.

Beta thalassemia occurs in people of Mediterranean origins, and to a lesser extent, Chinese and other Asian. Risk factors include a family history of thalassemia and an ethnic background susceptible to the disease. The incidence varies widely throughout the world.

Diagnosis of thalassemia:-

1. The diagnosis of beta-thalassemia minor usually is suggested by the presence of an isolated, mild microcytic anaemia, target cell on the peripheral blood smear, and normal red blood cell count. An elevated HbA2 demonstrated by electrophoresis confirms the diagnosis of beta-thalassemia. Elevated HbF level is not specific to the patient with beta-thalassemia trait.

Beta Thalassemia	HbF%	HbA%	HbA2%
Major	96	0	2-5
Intermedia	60-80	20-40	3-7
Minor	2-10	90-95	3-7

2- Free erythrocyte porphyrin (FEP) test may be useful in situations in which beta-thalassemia minor diagnosis is unclear.

3- Iron studies (S-iron, S.Ferritin, and T.I.B.C) are useful in excluding iron deficiency and the anaemia of chronic disorders as the cause of the patient's anaemia

4- The patient may require a bone marrow examination to exclude certain other causes of microcytic anaemia.

Bacteremia:-

Bacteremia is the presence of capable bacteria in the circulating blood (4). This may or may not have any clinical significance because harmless, transient bacteremia may occur following dental work or other minor medical procedures: however, this bacteremia is generally clinically benign and self-resolving in children who do not have an underlying illness or immune deficiency or a turbulent cardiac flow. The concern with occult bacteremia is that it could progress to a more severe local or systemic infection if left untreated. Most episodes of occult bacteremia spontaneously resolve, and serious sequence is increasingly uncommon. However, serious bacterial infections occur, including pneumonia, septic arthritis, osteomyelitis, cellulitis, and sepsis, possibly resulting in death. (2, 5).

Patients with occult bacteremia do not have clinical evidence other than fever (a systemic response to infection) (3). First described in the 1960s in young febrile children with unsuspected pneumococcal infection, bacteremia is defined as bacteria in the bloodstream or a febrile child who was previously healthy; the child does not clinically appear to be ill and has no apparent focus of infection. (5,6) Occult bacteremia has been defined as bacteremia not associated with clinical evidence of sepsis(shock or purpura) or toxic appearance, underlying significant chronic medical conditions, or clear foci of infection (other than acute otitis media) upon examination in a patient who is discharged and sent home after an outpatient evaluation(7).

Often, the only manifestation of occult bacteremia is fever or a minor infection (e.g., otitis media, upper respiratory tract infection)(4).

Therefore, in a busy clinic or emergency department, infants, and young children with occult bacteremia are difficult to distinguish from others in the waiting room. Fever is common in pediatric patients. Children average 4-6 fevers by age 2 years.

Fevers also prompt many visits to the pediatric clinic and emergency department. Approximately 8-25% of doctor's visits by children younger than 3 years are for fever, (4, 7, 8) 65% of children younger than 3 years visit a physician for acute febrile illness. (8) Fever is less common in infants younger than 3 months in those aged 3 months to 3 years. Young infants may not mount a fever response and may also be hypothermic in response to illness or stress. (7) Approximately 1% of infants younger than 2 months present with fever, and fever are twice as common in infants aged 1-2 months as in newborns younger than 1month. Of all pediatric patients presenting for fever evaluation, 20% have a fever for which the infection source is undetermined after a history and physical examination. Of all infants and young children

who present to the hospital for any reason, 1.6% appear nontoxic, were previously healthy, are older than 3 months, and have a fever without a source (9).

Bacteremia may also occur in children with focal infections or in children who have sepsis (i.e., clinical evidence other than the fever of a systemic response to infection.) Children with sepsis generally appear ill, have an increased heart rate or respiratory rate and may change in temperature (typically fever, although hypothermia is often seen in very young infants and newborns). Severe sepsis results in hypertension, hypoperfusion, or organ dysfunction. Septic shock occurs in children who do not respond to adequate volume resuscitation or requires vasopressors or inotropes. Although bacteria may present in the bloodstream of children with focal infections, sepsis, severe sepsis, or septic shock, this article's focus is occult bacteremia (10).

Pathophysiology

Much of the path physiology of occult bacteremia is not fully understood. The presumed mechanism begins with bacterial colonization of the respiratory passages or another mucosal surface; bacteria may egress into some children's bloodstream because of host-specific and organism-specific factors. Once viable bacteria have gained access to the bloodstream, they may be spontaneously cleared. They may establish a focal infection, or the infection may progress to septicemia; the possible sequelae of septicemia include shock and disseminated intravascular coagulation, multiple organ failure, and death. (4, 10)

Often, fever is the only presenting sign in patients with occult bacteremia and is defined as increased temperature caused by resulting in the thermoregulatory centre in the hypothalamus by the action of cytokines. (7)

The cytokines may be produced in response to viral or bacterial pathogens or by immune complexes. An increased temperature does not always represent a fever. (ll) Hyperthermia may also be due to increased heat production as it occurs in exercise or decreased heat loss as it occurs in over bundling, neither of which involves resetting the hypothalamic thermostat.

Clearly, some children are more susceptible to bacterial infection, which may initially be uncomplicated bacteremia but could rapidly lead to more serious complications. Immunosuppression due to neoplastic diseases or its treatment or splenectomized patient or defects in antibody responses or neutrophil responses predisposes certain children to invasive infection. Bacteremia should be considered, with a low threshold for evaluation and treatment, in patients with impaired immunity pr invasive medical devices such as indwelling central venous lines. The pathogen implicated in occult bacteremia change in response to vaccination against the common pathogenic strains. These changes govern the choices for empiric therapy of suspected bacteremia.

Risk factors

RACE: Studies of bacteremia prevalence in children in diverse settings have identified no racial, geographic, or socioeconomic predisposition (4, 6, 10). However, antibiotic resistance patterns vary in different geographic regions, affecting the treatment of children with bacteremia.

Sex: No sex-based difference in the prevalence or course of bacteremia is known (11)

Ape: Studies of occult bacteremia focus on children younger than 3 years. Some studies show that age does not affect the risk of developing occult bacteremia (12). At the same time, other analyses have found that variation in age-based risk depends on the infection organism.

Pneumococcal bacteremia is observed in children of all ages; however, children aged 6 months to 2 years are at an increased risk (12). The prevalence of pneumococcal meningitis peaks in infants aged 3-5 months. Meningococcal bacteremia occurs most frequently in infants aged 3-12 months; the highest risk of meningococcal meningitis is infants aged 3-5 months.(2,13) The risk of Salmonella bacteremia is greatest in infants younger than one year, especially in those younger than 2 months (2).

Season: A seasonal variation in febrile children presenting for evaluation is recognized. The peak is from late fall to early spring in children of all ages and is likely because of respiratory and Gl viral infections. Another peak occurs during the summer in infants younger than 3 months and is likely due to enteroviral infections and thermoregulation during hot weather.

Cause:

Causes of occult bacteremia vary depending on the age of the infant or child. Very young infants most commonly acquire infections from the mother during childbirth. As a patient's age increases, a gradual shift occurs toward community-acquired infections.
Older infants and children are at risk for bacteremia due to colonization of the nasopharynx or community-acquired organisms. Hib conjugate vaccine has decreased invasive Hib disease prevalence by 90% or more in industrialized countries. (2) With the disappearance of hib as a cause of occult bacteremia in children, the relative frequency of S Pneumoniae increased in some medical centres to more than 90%. (3) Since the introduction and widespread use of pneumococcal vaccines, the rate of vaccine-specific strains has dropped considerably, leading to significant changes in the patterns of causative organisms in more recent studies.
The prevalence of occult bacteremia caused by pneumococcus has greatly decreased since introducing the 7-valent conjugate pneumococcal vaccine, which was designed to cover 98% of the stains of S pneumonia responsible for occult bacteremia. (1) Multicenter surveillance found that 82-94% of S pneumonia invasive disease was caused by isolates in the 7-valent conjugate pneumococcal vaccine serotype invasive pneumococcal infection post-ILEC have dropped by 56%-100%, depending on location and age. (4, 2, 8, 10)

Aim of Study

To identify

1- Causative microorganism of bacteremia in febrile thalassemic patients in thalassemia care centre in Al-Zahraa Teaching hospital in Al-Najaf Al-Ashraf government.
2- Antibiotics sensitivity to that organism that is commonly used.
3- Factors that predispose significantly to bacteremia in thalassemic patients.

PATIENT AND METHODS

A total of the thalassemic patient in Al-Zahraa Teaching hospital in Al-Najaf Al-Ashraf government was 300 patients. We selected « 100 cases of febrile thalassemic patients from January 2009 to July 2009 were included in this study.

Patient and data collection

All patients taken by this study were febrile whose not proved any diagnosis that causes the fever, culture, and sensitivity before giving antibiotics.

For patients in these studies, data collections included age, sex, date of diagnosis, registration date, type of fever, pneumococcal vaccination, splenectomy and WBC count.

Specimen's collection and analysis:

Specimens were collected (according to the national committee for clinical laboratory standards (NCCLS) recommendations before the administration of antibiotics. Blood was cultured using brain heart infusion (Bhi) Broth (media used to propagate pathogenic cocci and other fastidious associated with blood culture work and allied pathological investigation. Blood is typically drawn from a vein by a needle with a syringe after the antiseptic technique. The site is cleaned with germ-killing medicine (antiseptic) by encircling the area with iodine, then wipe the area by spirit, usually from the inside of the elbow or the hand's back. May provider wraps an elastic band around the upper arm to apply pressure to the area and make the vein fill with blood; the blood collects into a small glass tube.

The area's pressure makes the vein fill with blood; it collects into a small glass tube. The blood sample mustn't become contaminated. We take 0.5ml of blood adding to 4.5ml brain heart infusion (BHI) broth, and the sample is sent to a lab in our hospital where it is placed in incubator oven at 37°C for 72 hours; after that, the specimen transferred to grow on culture agars (Blood, MC Conky, SS) Salmonella-Shigella) and chocolate agars for 24 hours in 37°C and watched to see if microorganisms
grew.

Micro organisms' identification by:-

1- Features of microorganisms growth on agars
2- Features of microorganisms under a microscope with a gram stain.
3- Further identification by standard biochemical tests (kligler, urea, mannitol, indol)
Antibiotic sensitivity test for gram-positive and negative bacteria included ampicillin, Amoxicillin, penicillin, cloxacillin, methicillin, amikacin, clindamycin, chloramphenicol, cefotaxime, vancomycin, gentamycin, cephalexin, Ceftriaxone and ciprofloxacin.

RESULTS

Seventy samples for blood culture was taken from a febrile thalassemic patient admitted to thalassaemic care centre during the period study (1st of February to the 1st of July), of whom 7 cases had proven bacteremia confirmed by positive blood culture.
The categorization data of the patient are given in:

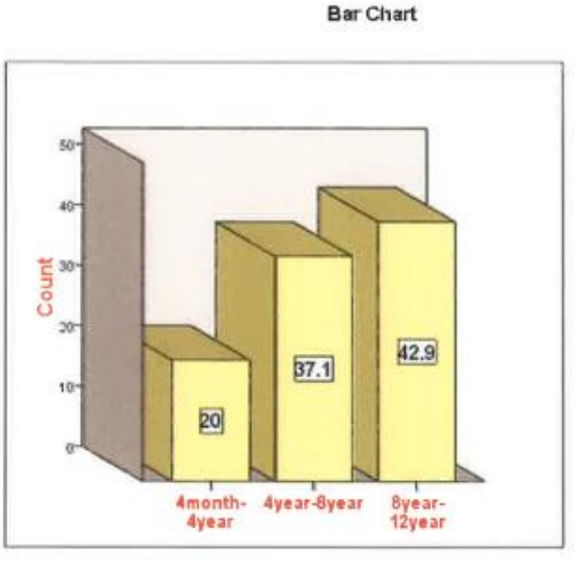

Diagram no.1

Diagram No. l: show the different age groups of patients included in the study, we found that the highest percent present in the age range from 8-12 years (42.9%).

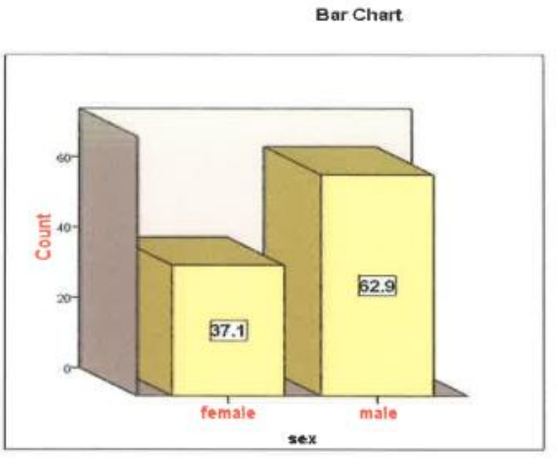

Diagram no. 2

Diagram no. 2: show the sex distributions of patients included in the study the result was the male (62.9%) and the female (37.1%).

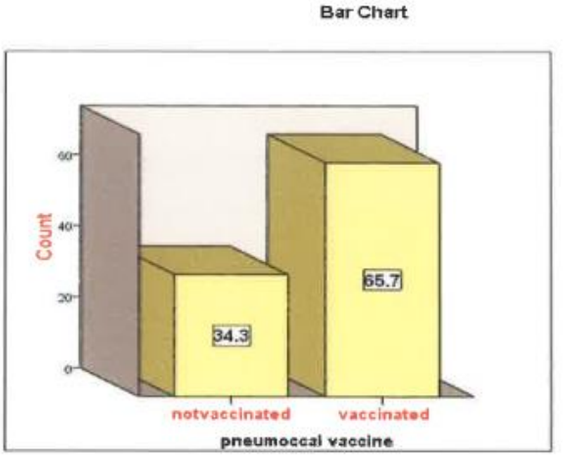

Diagram no.3

Diagram no. 3: show the pneumococcal vaccine received by patients included in the study

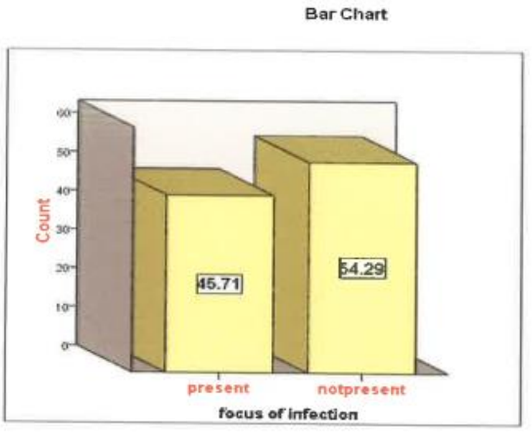

Diagram no. 4

Diagram no. 4: show the focus of infection in the patients included in the study (54.29%) without the focus of infection

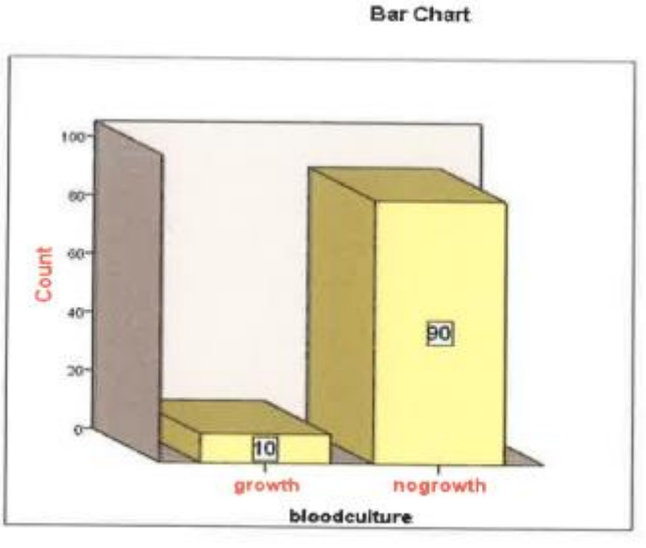

Diagram no.5

Diagram no.5: show the percent of the patient with positive blood culture 90% with no growth.

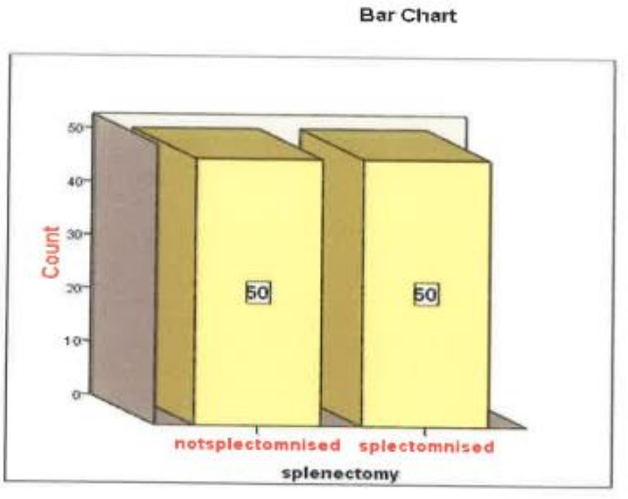

Diagram no.6

Diagram no. 6: show the splenectomy in patients included in the study; 50% of patients were splenectomized.

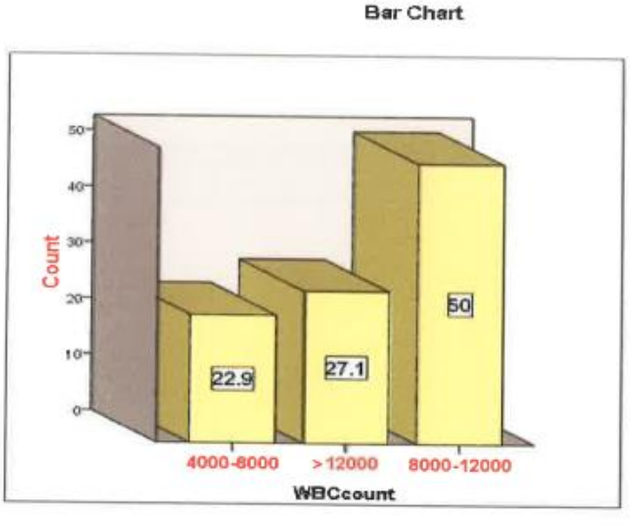

Diagram no. 7

Diagram no.7: show the WBC count of the patients included in the study.

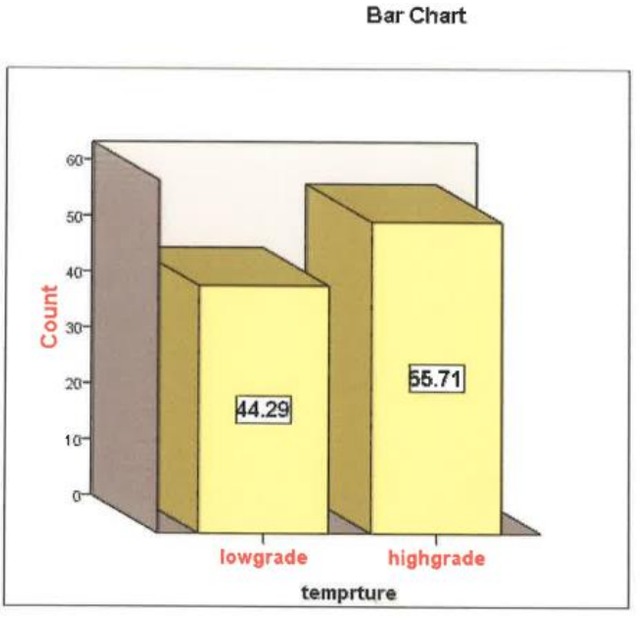

Diagram no.8

Diagram no. 8: show the type of fever in the patients included in the study (55.7%) with high-grade fever.

Table No. l: the relationship between bacteremia (positive blood culture) and sex

		sex	
		male	female
growth	Count	4	3
	% within sex	9.1%	11.5%

P value =0.744

Table no.2 the relationship between: bacteremia (positive blood culture) with age.

		age		
		4month-4year	4year-8year	8year-12year
growth	Count	1	4	2
	% within age	7.1%	15.4%	6.7%

P value =0.526

Table no. 3: the relationship between bacteremia (positive blood culture) and the type of fever.

		temperature	
		low grade	high grade
growth	Count	1	6
	% within temperature	3.2%	15.4%

P value =0.074

Table no. 4: the relationship between bacteremia (positive blood culture) count

		WBCcount		
		4000-8000	8000-12000	>12000
growth	Count	0	4	3
	% within WBCcount	.0%	11.4%	15.8%

P value= 0.131

Table no. 5: the relationship between bacteremia (positive blood culture) and focus of infection

		focus infection	
		not present	present
growth	Count	5	2
	% within focus infection	13.2%	6.2%

P value =0.328

Table no. 6: percentage of bacteremia with pneumococcal vaccine (p value=0.734)

		pneummoccocalvaccin	
		vaccinated	not vaccinated
growth	Count	5	2
	% within pneummoccocalvaccin	10.9%	8.3%

Table no.7: the relation between becteremia and splenctomy

	splenectomy	
	Splenctom - ised	Notsplenctomi-sed
growth Count	6	1
% within splenectomy	17.1%	2.9%

P value = 0.037

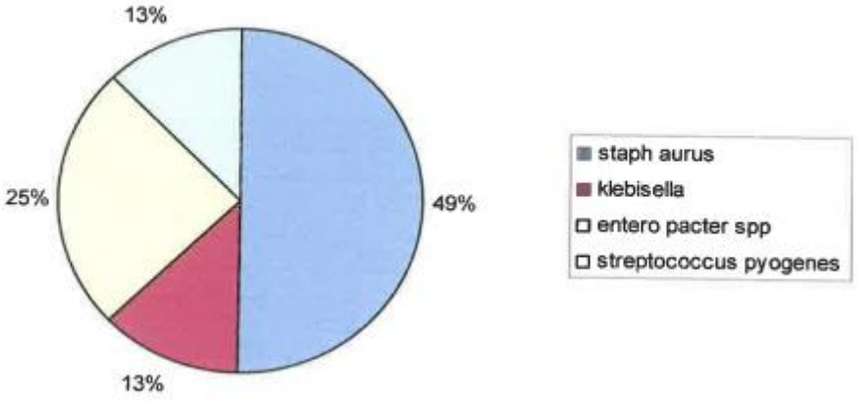

Diagram no. 9: show the percent of microorganisms in patients with positive blood culture

DISCUSSION

Bacteremia is one of the serious problems in thalassemic patients; in our study, the percentage of patients with Bacteremia was 10%; this was probably due to difficulties in getting positive in laboratory work and a negative sample might be due to viral or other microorganisms.

In our study we found that 42.9% of the patient was in the age group 8-12 years, this primarily due to most of the patient in this age group was splenectomized and some of them not complete their vaccination and not taken benzathine penicillin regularly after splenectomy

The percentage of bacteremia is higher in male, 62.9%, while in female, 37.1%; this may be due to the family healthcare style we found that 55.7% had a high-grade fever (defined as body temperature 39.5-40.5 C°). This is primarily due to the thalassemic patient is immune-compromised and are more liable for bacterial infection.

In our study, 17.1 % of patients with the growth of bacteria were splenectomized; bacteremia should be put with a high index of susception for evaluation and treatment of thalassemic patients because of impaired immunity.

CONCLUSION

1. Bacteremia percentage was 10 %.
2. The most common organism was Staphylococcus, although there are another gram-positive and gram-negative bacteria.
3. Bacteremia in this study was as follows:
    a) Both sexes are susceptible, and male commonly affected than female.
    b) The most affected age group was between 8-12 years (42.9%).
    c) Fifty per cent was splenectomised.
    d) The highest per cent (55.7%) was with high-grade fever.

e) Regarding WBC count, the highest percentage, 50%, was between (8000 -12000).

RECOMMENDATION

To decrease the risk of bacteremia in the thalassemic patient:-

1. each febrile thalassemic patient should have a blood culture, especially Splenectomised patient.
2. If blood culture is not available, all febrile thalassemic patient, especially Splenectomised, should receive broad-spectrum antibiotic because of the risk of bacteremia.
3. Early detect signs and bacteremia symptoms to make a critical decision without life-threatening delays, blood should be sent for culture and sensitivities and immediate use of antibiotics accordingly.
4. Educate the mothers about early signs and symptoms of bacteremia, and immediate consultation should be made.
5. Encourage the parents about the impotence of regular visit to the thalassemic care centre to avoid risk factors that increase the mortality rate of sepsis.

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