



The Role of Vancomycin on Meningitis

Menenjitte Vankomisinin Etkisi

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ABSTRACT

Purpose: Central nervous system(CNS) infection is the most common cause of fever associate with signs and symptoms of CNS disease in children. Many organisms can cause these infections, but viral is the most common, then bacterial which is more common than parasitic and fungal infections. The most common three organisms are Haemophilus influenza type b(Hib), streptococcus pneumonia and Nieseria meningitis. Treatment should start as soon as possible in bacterial meningitis with antibiotics, but there is no need for antibiotics in viral meningitis. The antibiotics used third generation cephalosporines, penicilinge G, vancomycin, chloramphenicol .the duration of therapy ranges from 7-14 days, but in case of vancomycin it ranges from 5-7 days. The aims of this study were; to estimate the role of vancomycin in treatment of meningitis, to evaluate the role of antibiotics used in treatment of meningitis with special focus on vancomycin, to elaborate a guideline ladder for meningitis treatment depend on the type of organism and to establish a reliable and applicable plane for diagnosis of meningitis in Gaza.

Material and Methods: The study conducted in Dorrah Hospital in Gaza between 1/9/2011 – 31/11/2011 designed retrospective study. All the archives for children diagnosed meningitis in this period were included in this study. The total number of patients was (85), of whom two were excluded .one died after two hours of hospital arrival and the other due to incomplete information in the archive. The data collected were tabulated and analyzed with spss version 13. The value of $P < 0,05$ were considered statistically significant. We used independent T- test to compare between means.

Results: All the cases treated whether using vancomycin or without vancomycin were improved. There were no difference between patients used vancomycin with other drugs and those do not use it, conversely patients do not receive vancomycine have better outcome. This means most of the cases do not need vancomycin as essential therapy. We found that the outcome regarding to the hospital stay was better in patients who do not treated with vancomycin. This confirmed by (58%) stayed in the hospital 5-7 days or less and 28% stayed 4 days or less. In general 86% of cases stayed less than 8 days. The study in case of bacterial infection, the number of cells in CSF is higher than a septic , while the sugar elevation is higher than in the aseptic form of meningitis and the culture is negative. The results revealthat the majority of cases were aseptic 71% with the cells number below 300. This result is confirmed by the criteria considered for a septic meningitis in Nelson text book of pediatrics. The study found that meningitis affects small age children and most of cases present in the age range from 3,1 month and 5 years, 56% of cases aged between 3,1-24 month and 20% aged 24,1-60 month. The total percent is 76% ranges from 3,1-60 month.

Conclusion: After the previous discussion of the results obtained from this study, the researchers concluded that most of the cases diagnosed meningitis was aseptic and there was no need for antibiotics. Also in those who diagnosed as bacterial vancomycin was not essential in all cases, this confirmed by the absence of any differences in the outcome.

Keywords: Meningitis, vancomycin, bacteria, virus, antibiotics.

ÖZET

Amaç: Merkezi sinir sistemi (CNS) enfeksiyonu, çocuklarda meydana gelen CNS hastalığının semptomları ve belirtileri ile ilişkili ateşin en yaygın nedenidir. Organizmaların çoğu bunun gibi enfeksiyonlara neden olabilir. Ancak; en yaygın viral enfeksiyonlardır. Daha sonra sırasıyla bakteriler, parazitler ve mantar enfeksiyonları gelmektedir. En yaygın 3 organizma; Haemophilus influenza (Hib), streptococcus pneumonia ve nieseria meningitis'tir. Antibiyotik tedavisi bakteriyel menenjit vakalarında mümkün olan en kısa zamanda başlatılmalıdır. Ancak viral menenjitte antibiyotik tedavisine gerek yoktur. 7-14 günlük tedavi süresinde kullanılan antibiyotikler; sefalosporinler, penisilin G, vankomisin, kloramfenikol olmakla birlikte vankomisin 5-7. günler arasında kullanılmaktadır. Bu çalışmanın hedefleri menenjit tedavisinde vankomisin rolünün belirlenmesi, vankomisin odaklı menenjit tedavisinde kullanılan antibiyotiklerin rollerinin değerlendirilmesi, organizmanın tipine göre uygulanan menenjit tedavisinin aşamalarını önceden belirlemek ve Gaza'da menenjitin teşhisi için güvenilir ve uygulanabilir planı tanımlamak

Materyal ve Metod: 1 Eylül-31 Kasım 2011 tarihleri arasında Gaza'da Dorrah hastahanesinde yürütülen bu çalışma geçmişe yönelik çalışma olarak tasarlanmıştır. Bu periyotlar arasında menenjit tanısı konmuş tüm çocuklar çalışmaya dahil edildi. 1 hasta hastaneye geldikten sonra öldüğünden, diğerinin ise bilgilerinde eksiklik olduğundan dolayı 2 hasta çalışmadan çıkarıldı ve böylece çalışmaya dahil edilen toplam sayı 85'ti. Toplanan bilgiler tablo haline getirildi ve SPSS 13 programı ile analizleri yapıldı. P değeri 0.05'ten az çıktığı için çalışma bulguları istatistiksel olarak anlamlıydı. Değerleri karşılaştırmak için bağımsız T-testi uygulandı.

Bulgular: Tüm vakaların vankomisinli mi yoksa vankomisinsiz mi iyileştirildiği değerlendirildi ve vankomisin kullananlar ile diğer ilaçları kullananlar arasında herhangi bir farklılık gözlenmedi. Diğer taraftan vankomisin almayan vakalarda daha iyi bir iyileşme gözlemlendi. Bu da demek oluyor ki; vakaların çoğunun vankomisin tedavisine herhangi bir şekilde ihtiyaç duymuyordu. Hastane sonuçlarına göre vankomisin tedavisi uygulanmayan hastaların daha iyi olduğunu bulduk. 5-7 gün veya daha az hastanede kalanların %58'i ve 4 gün veya daha az kalanların ise %28'inde bu sonuçlar bulundu. 8 günden daha az hastanede kalan vakaların ise %86'sında aynı sonuç bulundu. Bakteriyel enfeksiyon vakasında; şeker seviyesi menenjitin aseptik formundan daha yüksek ve kültür negatif iken CSF'de ki hücrelerin sayısı septikten daha yüksekti. Vakaların büyük bir çoğunluğu 300'ün altında hücre sayısı ile %71 aseptiktik olduğunu ortaya koymaktadır. Bu sonuçlar; pediatriğin Nelsen text kitabında septik bir menenjit için değerlendirilen kriterler ile doğrulandı. Bu çalışmada; menenjitin küçük yaştaki çocukları etkilediği ve vakaların çoğunun 3,1 aylık-5 yaş aralığında olduğu bulundu. Vakaların %56'sı 3,1-24 aylık yaşlarında iken %20'si 24,1-60 aylık yaş aralığındaydı. Yani 3,1-60 aylık yaş aralığında ki vakaların toplam yüzdesi %76 idi.

Tartışma: Bu çalışmadan derlenen sonuçlardan sonra araştırmacılar; menenjit tanısı konulmuş vakaların çoğunun aseptik olduğu ve antibiyotik tedavisine ihtiyaç duyulmadığı sonucunu çıkardılar. Aynı zamanda bakteriyel sebepli menenjit vakalarının hepsi için dahi vankomisine gerek olmadığını belirlediler. Bu, vankomisin yokluğunda herhangi bir değişikliğin olmaması ile doğrulandı.

Anahtar Kelimeler: antibiyotik,bakteri, menenjit, vankomisin, virüs,

INTRODUCTION and LITERATURE REVIEW

Central nervous system(CNS) infection is the most common cause of fever associate with signs and symptoms of CNS disease in children. Many organisms can cause these infections, but viral is

the most common, then bacterial which is more common than parasitic and fungal infections¹. Regardless the etiology, most of the patients have similar signs and symptoms such as, headache, vomiting, fever. The most common three organisms are Haemophilus influenza typeb(Hib), streptococcus pneumonia and Nieseria

meningitis. The most potential infections is meningitis (bacterial meningitis). The introduction of vaccine against (Hib) and *S. pneumoniae* reduce the infection 59%^{2,3,4}. In the United States of America, there is vaccines against some strains of *Neisseria meningitidis*. This vaccine is sometimes used to control outbreaks of some types of meningococcal meningitis⁵. Despite advances in antimicrobial and general supportive therapies, central nervous system (CNS) infections remain a significant cause of morbidity and mortality in children. It has a high rate of acute complication and long term morbidity³. The diagnosis of acute pyogenic meningitis is confirmed by analysis of the CSF, which typically reveals microorganisms on Gram stain and culture, a neutrophilic pleocytosis, elevated protein, and reduced glucose concentration. Lumbar Puncture (LP) should be performed when bacterial meningitis is suspected. Treatment should start as soon as possible in bacterial meningitis with antibiotics, but there is no need for antibiotics in viral meningitis. The antibiotics used third generation cephalosporines, penicillin G, vancomycin, chloramphenicol. The duration of therapy ranges from 7-14 days, but in case of vancomycin it ranges from 5-7 days¹. The administration of vancomycin in meningitis is controversial, some studies reveal that concomitant use vancomycin with steroids reduce vancomycin penetration to cerebrospinal fluid (CSF), while others deny these results. Others encourage use of vancomycin despite the previous effect because it can reduce the incidence of neurological sequel. This finding should be kept in mind, especially after the increase of pneumococcal serotype 19A that has led to increased antimicrobial resistance to β lactams^{6,7,8,9,10,11,12}. Vancomycin is of value in a number of serious diseases such as endocarditis and meningitis. However, it is often necessary to combine vancomycin with other antibiotics, such as ceftriaxone for synergistic effects when treating meningitis^{13,14}. In a study to evaluate vancomycin in hospitalized children show that only 7% had

laboratory-confirmed β -lactam-resistant organisms isolated at the time vancomycin was prescribed¹⁵. Another study concluded that early empiric vancomycin therapy was not clinically beneficial in children with pneumococcal meningitis but was associated with a substantially increased risk of hearing loss. It may be prudent to consider delaying the first dose of vancomycin therapy until 2 hours after the first dose of parenteral cephalosporin in children beginning therapy for suspected or confirmed pneumococcal meningitis¹⁶. The Canadian Society of Pediatrics conducted a study to introduce an algorithm for meningitis. It recommends that Gram stain, if it is examined by an experienced reader, may help point to the bacterial species involved. However, therapy should not be based on the results of the Gram stain alone. Previous oral antibiotic use can reduce the yield in finding the etiological bacterial agent in both the CSF Gram stain and culture. Once the responsible organism is subsequently identified from blood or CSF and the antibiotic susceptibilities are known, the most appropriate antibiotic treatment may be selected to complete the full course of therapy. If the responsible organism is not isolated on culture, then the antibiotic treatment chosen for empirical therapy may be used to complete the course of therapy¹⁷. In a large study conducted in USA it makes guidelines for meningitis and considered vancomycin as empiric therapy for meningitis. While according to the British NICE guideline for meningitis treatment vancomycin is not empirical except in people who travelled outside England and exposed to long term treatment with antibiotics¹⁸.

Aims

1. Estimate the role of vancomycin in treatment of meningitis.
2. Find out the percentage of complications and treatment failure.
3. Considering this study as a base line for other randomized clinical trials on vancomycin and meningitis treatment.

Methodology

The study conducted in Dorrah Hospital in Gaza between 1/9/2011 – 31/11/2011 designed retrospective study. All the archives for children diagnosed meningitis in this period were included in this study. The inclusion criteria was meningitis based on lab study, clinical examination and gram stain, all patients must be inpatient. The patients age were 1month- 12 years. Any other patients do not obey this criteria will be excluded. The data

then extracted from the archives see(annex1). The total number of patients was (85), of whom two were excluded .one died after two hours of hospital arrival and the other due to incomplete information in the archive. The data collected were tabulated and analyzed with spss version 13. The value of $P < 0,05$ were considered statistically significant. We used independent T- test to compare between means.

RESULTS

Table 1. Compares the hospital stay for both drugs, it is statistical significant but the mean is better in cases of treatment without vancomycin.

drug	N	Mean	Std. Deviation
vancomycin	17	1	0
Without vancomycin	66	2.09	0.518
P- Value= 0.0			

Table 2: show that patients treated with vancomycin needs follow up more than the other group.

drug	N	Mean	Std. Deviation
vancomycin	17	2	0
Without vancomycin	66	1.88	0.33
P- Value= 0.004			

Table 3: discuss the re lumbr puncture in both groups, it is clear that patients treated with vancomycin needsre lumbr puncture more than the other group.

drug	N	Mean	Std. Deviation
vancomycin	17	2	0
Without vancomycin	66	1.99	0.173
P- Value= 0.03			

Table 4: represent the between bacterial and aseptic meningitis in relation to the number of cells, it is clear that the bacterial type is associated with high number.

Disease type	N	Mean	Std. Deviation
aseptic	59	1.15	0.36
bacterial	24	4.04	0.91
P- Value= 0.012			

Table 5: represent the between bacterial and aseptic meningitis in relation to the sugar %, it is clear that the a septic type is associated with high percent.

Disease type	N	Mean	Std. Deviation
aseptic	59	3.16	0.87
bacterial	24	1.75	0.44
P- Value= 0.0			

Table 6: represent the between bacterial and aseptic meningitis in relation to the culture, it is clear that the a septic type have negative culture.

Disease type	N	Mean	Std. Deviation
aseptic	59	3	0.33
bacterial	24	2.67	0
P- Value= 0.03			

DISCUSSION

Central nervous system(CNS) infection is the most common cause of fever associate with signs and symptoms of CNS disease in children. The most potential infections is meningitis (bacterial meningitis) The introduction of vaccine against (Hib) and S. pneumonia reduce the infection 59%. The most common three organisms are Haemophilus influenza typeb(Hib), streptococcus pneumonia and Nieseria meningitis^{2,3,4}. In this retrospective study we tried to evaluate the role of vancomycin in the treatment outcome of meningitis.

Improvement and outcome

All the cases treated whether using vancomycin or without vancomycin were improved figure (1). Table^{2,3} shows that there is no difference between patients used vancomycin with other drugs and those do not use it, conversely the mean value shows that patients do not receive vancomycine have better outcome. Also figure 5 show that only 20% of patients received vancomycin. This means most of the cases do not need vancomycin as essential therapy.

Hospital stay

If we look to table², p –value=0, it is extremely statistical significant, but if we compare the means, we found that the outcome regarding to the hospital stay was better in patients who do not treated with vancomycin. This confirmed by figure

1, which reveal that the majority of cases(58%) stayed in the hospital 5-7 days or less and 28% stayed 4 days or less. In general 86% of cases stayed less than 8 days. This may mean that 7 days is enough for meningitis treatment with some exceptions.

Type of organism

Looking to the tables^{4,5,6} P-value were statistically significant, but the mean value in table 5 show that the number of cells in CSF in bacterial is higher than a septic infection , while in table 6, the sugar elevation is higher than in the aseptic form of meningitis and the culture is negative in table 5. This result confirmed by figure 3 and figure 4. Figure 3 show that 71% of cases are aseptic confirmed by figure 4 show that 71% of cases have cells number below 300. This result is confirmed by the criteria considered for a septic meningitis in Nelson text book of pediatrics¹.

Age groups

Figure 5 show males affect more than females this may be due to their exposure to the outer hygiene more than females. Figure 7 show that meningitis affects small age children and most of cases present in the age range from 3,1 month and 5 years. This table reveals that 56% of cases aged between 3,1- 24 month and 20% aged 24,1-60 month. The total percent is 76% ranges from 3,1-60 month.

Conclusion and recommendations

After the previous discussion of the results from this study, the researchers concluded that most of the cases diagnosed meningitis was aseptic and there was no need for antibiotics. Also in those who diagnosed as bacterial, vancomycin was not essential in all cases. This confirmed by the absence of any differences in the outcome, so the researchers recommended the following:

1. Polymerase chain reaction (PCR), or at least coagulation test should be done before administration of antibiotics. This will confirm the diagnosis of the type of organism (bacterial or viral) results in reduction in misuse of antibiotics and cost effective treatment regime. The exception only is serious cases where the clinical diagnosis mostly confirm bacterial meningitis.
2. Improve the quality of laboratories performance through equipment, media, and technician development.
3. Two isolation room in each department must be present one for bacterial and the other for aseptic form of meningitis. This reduces the cross infections since aseptic form only requires fluid replacement and antipyretic drugs while bacterial needs antibiotics also.
4. Vancomycin should administer as empiric therapy only after (PCR) or confirmation of streptococcal pneumonia, staphylococcus, patients diagnosed meningitis and appear toxic or if there is no improvement on ceftriaxone or cefotaxime after 48 hours.
5. If PCR or agglutination test is not available, bacterial meningitis should be ceftaxime or cefotaxime used alone as empiric therapy in all causes of meningitis (age group 3m – 12 years). For patients Aged 1-3 months use as empiric therapy ampicillin with cefotaxime.
6. Vancomycin should administer as empiric therapy only when bacterial meningitis is most likely (cell > 1000 , protein > 60mg/dl , sugar < 40mg/dl or less than 50% of serum glucose)
7. Treatment with vancomycin should only continue for five days then stop, this because vancomycin only passes blood brain barrier during inflammation. After inflammation cures vancomycin does not pass.
8. Conducting another randomized clinical trial to evaluate the role of vancomycin in meningitis in Gaza strip. This is helpful in establishing guidelines for meningitis treatment.

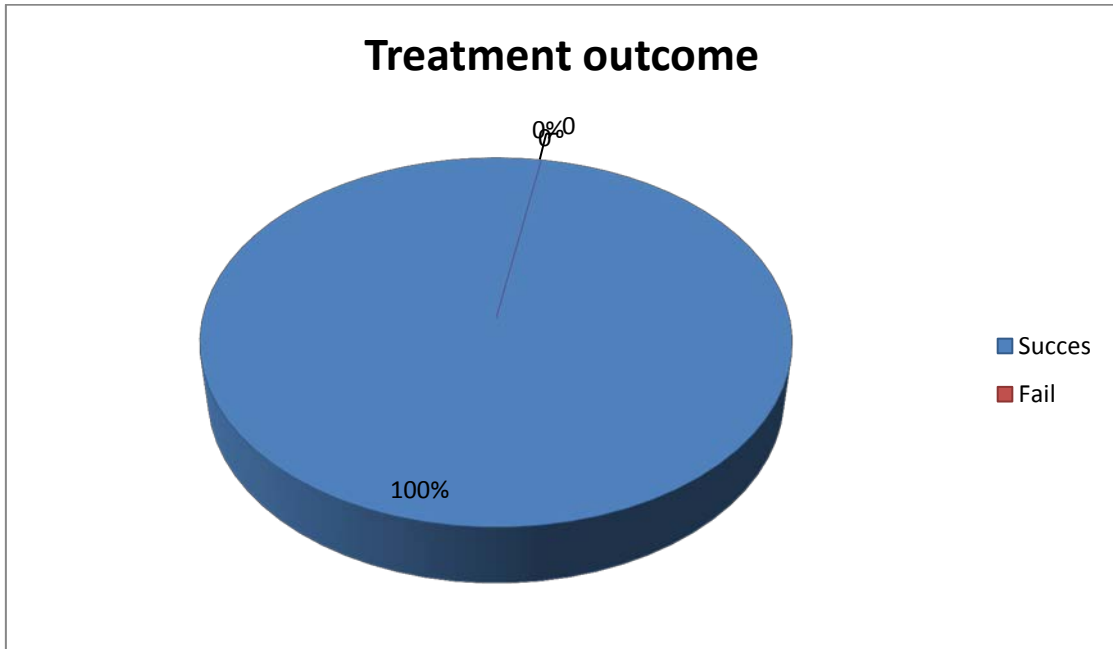


Figure 1. Show that successful treatment is 100% and failure is 0%

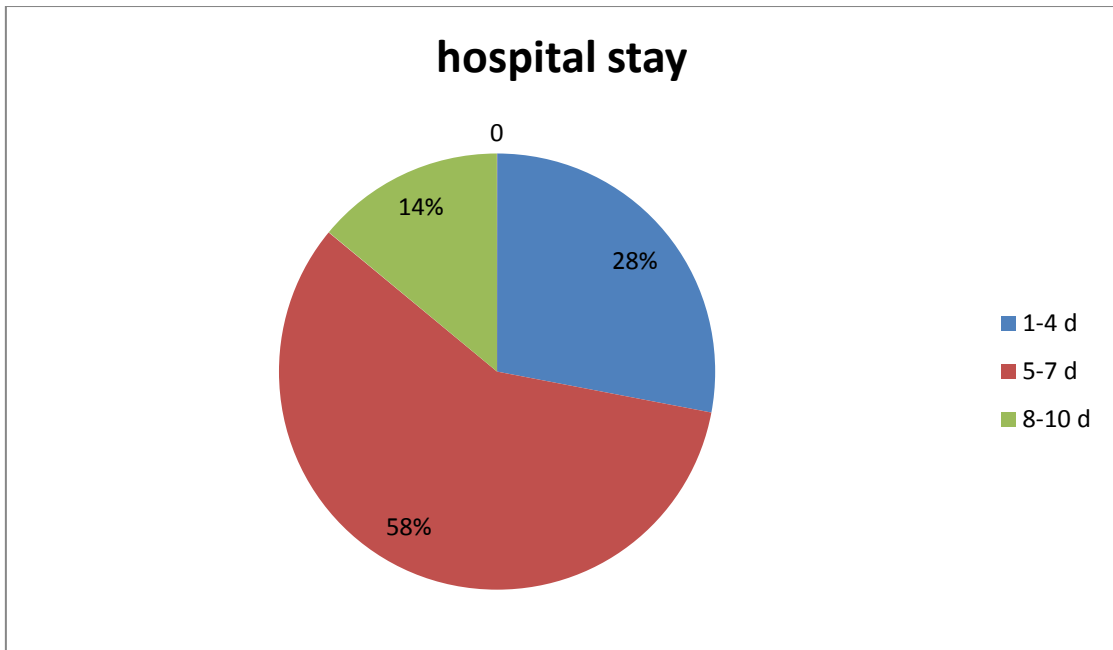


Figure 2. Shows that only 14% of cases continue treatment 8-10 days while the rest ranges from 4-7 days.

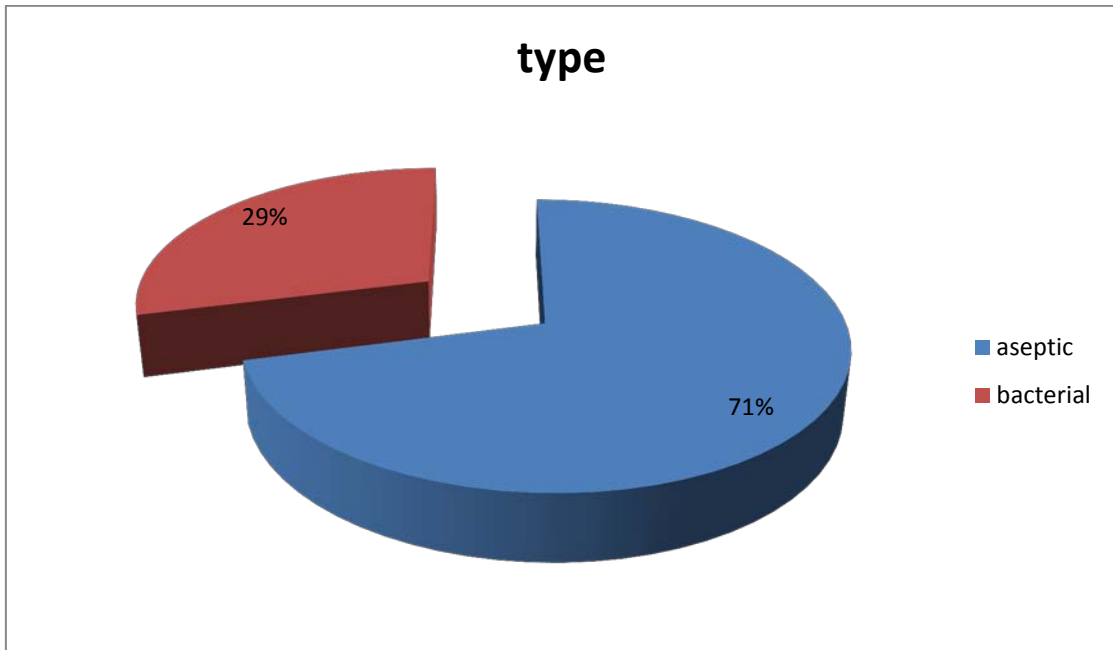


Figure 3. It is clear from this figure that aseptic form is 71% and bacterial is 29%.

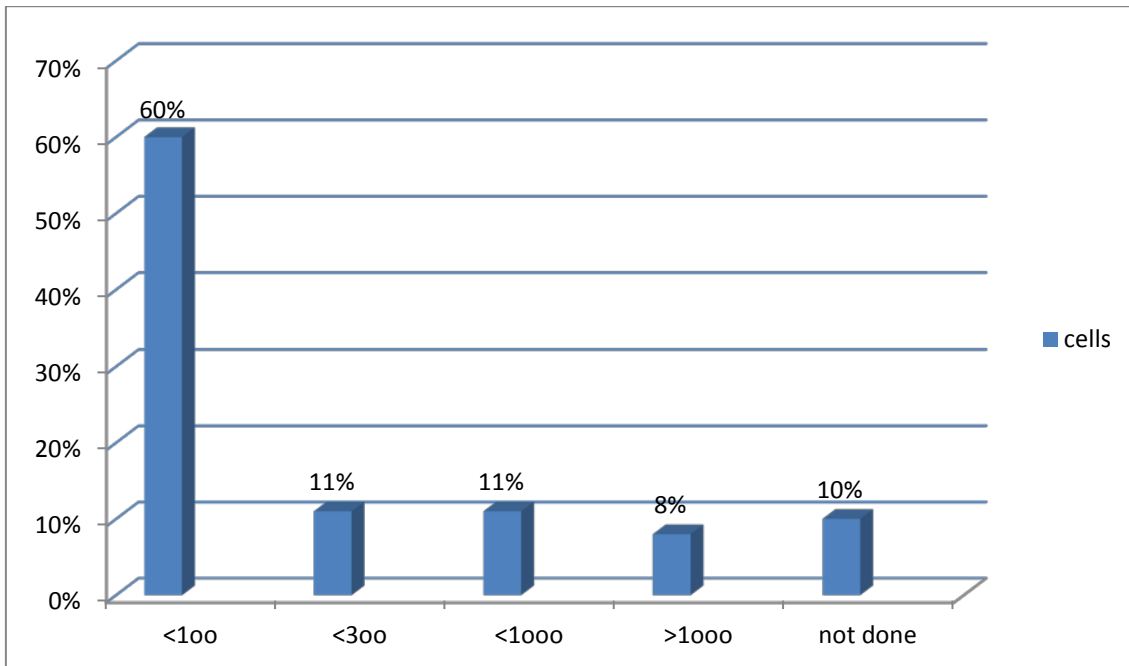


Figure 4. Shows that the majority of cases have low number of cells 71% below 300 which confirm that a septic form in previous figure 71%. Confirmed by Nelson text book of Ped.

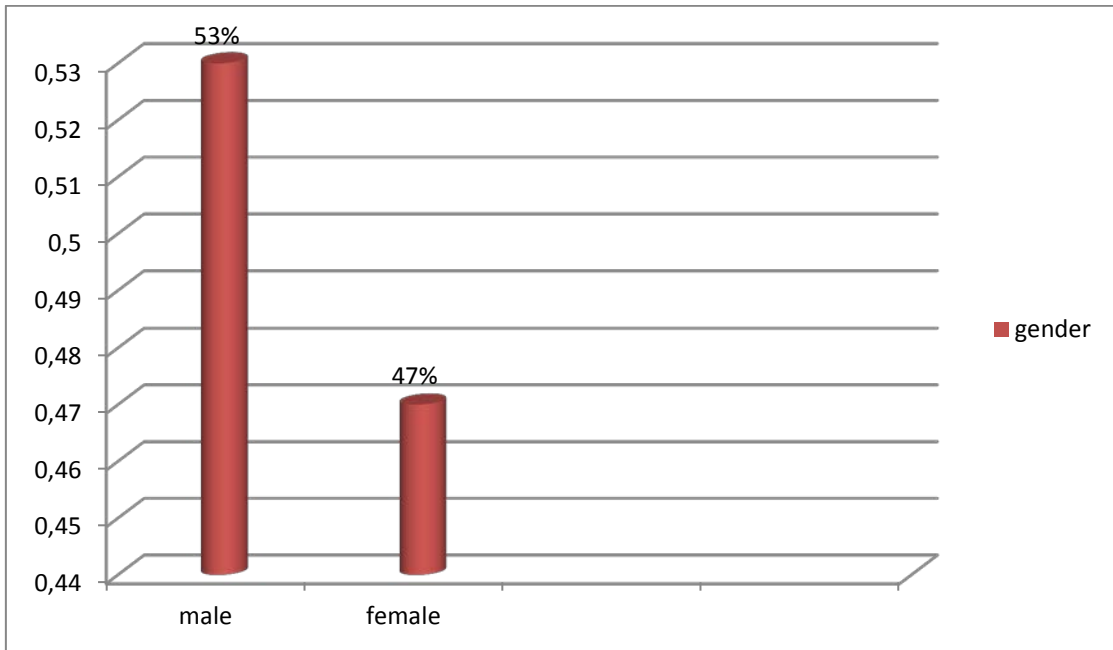


Figure 5. Shows that the incidence of meningitis in males is higher than females.

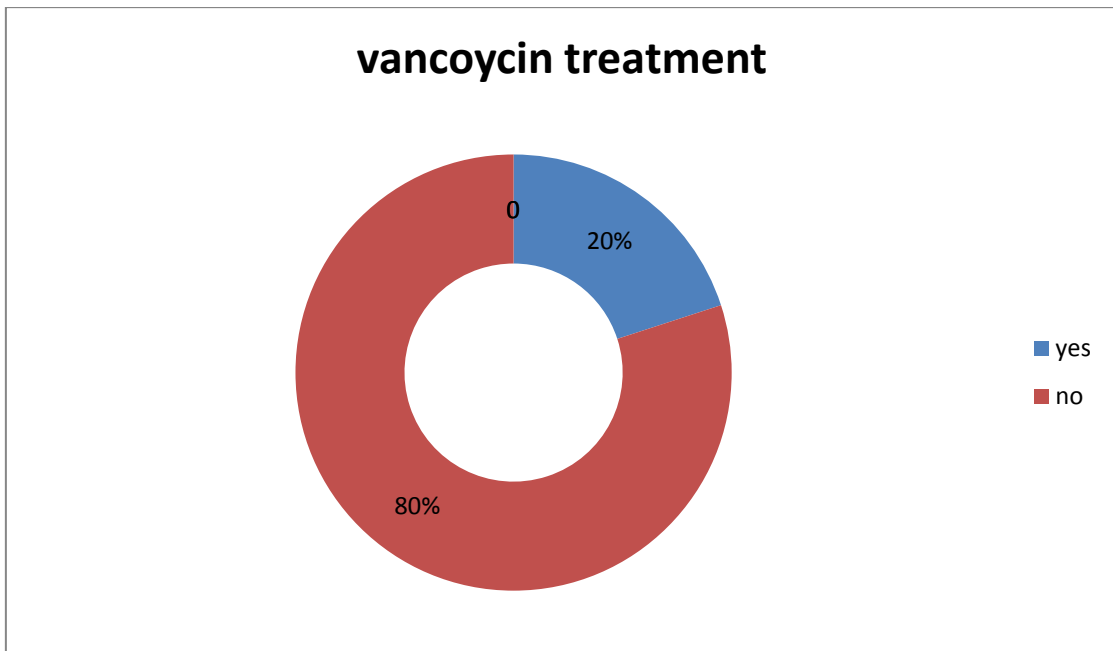


Figure 6. From this figure 20% of patients received vancomycin along with other drugs and 80% do not use it.

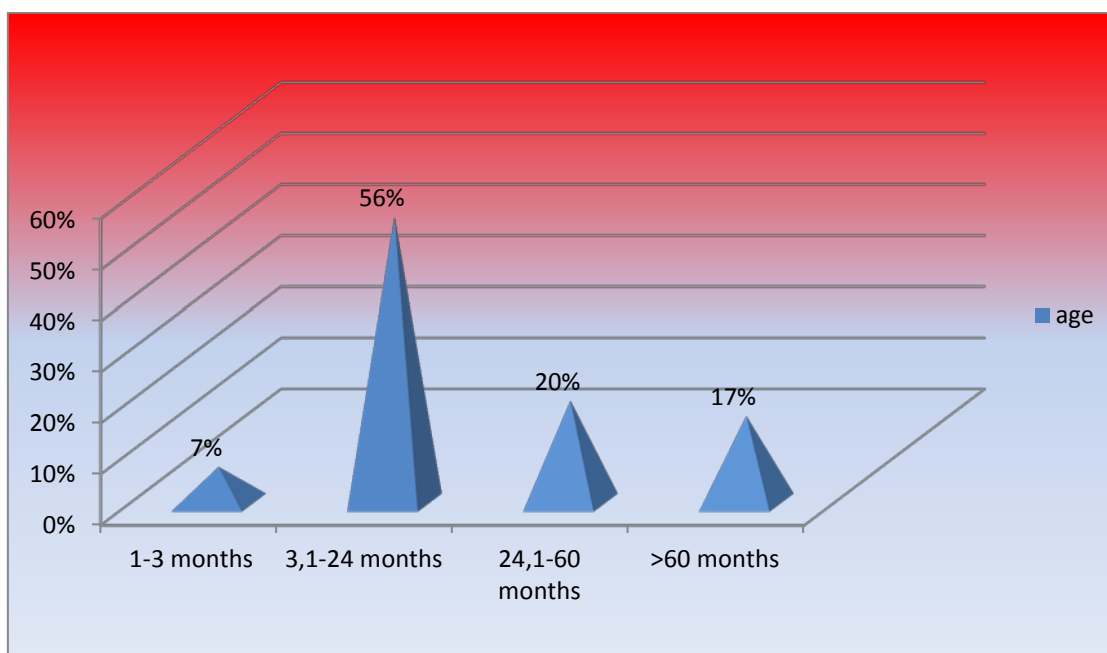


Figure 7. The highest incidence rate is in children aged 3.1 month and 5 years and the highest percent is in the age 3.1-24 months

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