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Procalcitonin, The Most Reliable Biomarker For Early Diagnosis Of Bacterial Septicaemia.

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Abstract

Septicaemia, a life threatening infection, caused by invasion of virulent microorganism into blood stream. It is characterized by whole body inflammation, leads to multi-organ dysfunction, resulting in high mortality rate. Immunocompromised patient with Cancer, ICU patient or patient with severe burns becomes more susceptible with its complication. Therefore early diagnosis & anti-microbial therapy is highly important in reducing morbidity & mortality. Unfortunately there are no such gold standard diagnostic method for early diagnosis & therapeutic intervention. In this review I focus the dependence on serum bio-marker for early diagnosis as delay in anti-biotic therapy increases mortality by 7.6%/ hour in patient with septicaemia. But conventional markers like CRP, lactate, BNP and other haematological studies like ESR, Total WBC count etc. are not Specific. To eliminate late diagnosis, serum biomarker Procalcitonin is found to be superior and most reliable. PCT is produced by numerous organ after bacterial pro-inflammatory stimulation and level increases 2-4 hours after bacterial infection. It can be detectable for upto 7 days and level decreases with successful treatment. Mild elevation is seen in viral infection and severe rises seen in bacterial sepsis. Further research work is needed for declaring a gold standard test for sepsis.

Keywords:- Immunocompromised , Inflammation, Mortality, Procalcitonin, Septicaemia.

Introduction:-

Septicaemia or bacterial sepsis is an infectious disease caused by bacteria. Most common source of this infection is lung infection followed by abdomen and urinary tract. In a recent analysis about 31.5 million cases are reported globally for septicaemia. In India it is a major burden and also the mortality to sepsis is as high as 56.2% depending on type of organism involved (Markus and Peter, 2013). It is well known to all that septicaemia is associated with high morbidity & mortality, so early diagnosis is mandatory to cure it accurately. On the other hand its clinical characterization by investigating physiological parameter such as temperature, pulse rate, respiratory rate, total white blood cell count etc. is too complex. However, at early state it shows

several non-specific and non-sensitive signs, therefore primarily septicaemia diagnosis is immense challenging to physician (Wacker and Prkno, 2013).
Unfortunately there are no such gold standard test to diagnose septicaemia. As we know bacteria are the most common agent for sepsis and bacterial identification by conventional method i. e. bacterial culture turn out to be positive in only 50 % cases (Hillas et al., 2010). To take any therapeutic decision from blood culture requires minimum 24-48 hours. In addition molecular techniques can't differentiate between true infection and contamination. Although molecular techniques are very costly (Vijayan et al., 2017). Other conventional approaches such as C-reactive protein (CRP) or white blood cell count are not so specific to septicaemia and have some limitation (Liu et al., 2015).
In India it is reported that ICU patients are more prevalent to sepsis, about 28.3% patient acquire septicaemia when they stay in ICU (Zhao and Dong, 2017). Also, the diagnosis of infection of those critically sick patients is very challenging by traditional method.
Therefore we have to dependent on serum bio-marker for early diagnosis and start anti-biotics therapy to reduce mortality.

Role Of PCT:-

Procalcitonin seek much attention day by day as a bio-marker for septicaemia (Gregoriano et al., 2020). Actually PCT is a precursor hormone of calcitonin and normally it is undetectable in healthy individual. The release of PCT is upregulated by the inflammatory response caused by bacteria and surprisingly downregulated during recovery (Covington et al., 2018). So the PCT secretion indicates the severity of inflammation, higher level is associated with more severe infection and declining level indicates recovery of illness (Müller et al., 2001).
Normal reference value of PCT is less or equal to 0.15 ng/ml. The level between 0.15 – 2.0 ng/ml does not conclude such infection but the level > 2.0 ng/ml suggest any systemic bacterial infection or sepsis (Hammond et al., 2022). Although higher level of PCT value may not always associated with systemic bacterial infection (Angus et al., 2013).
Pathophysiology of PCT in Sepsis :-
Actually the secretion of procalcitonin in case of bacterial sepsis is not well known but it assumes that PCT prefers to secrete either directly or indirectly by alternate pathway (Lever and Mackenzie, 2007). During sepsis mainly gram-negative bacteria and their antigens stimulate several anti-inflammatory mediators. These anti-inflammatory mediators – cytokines like IL-2, IL-6, TNF-α and bacterial lipopolysaccharides modulate the liver cells and mononuclear blood cell like monocytes and macrophages to secrete PCT (Fleischmann et al., 2016). As we know in healthy individual, procalcitonin is produced by parafollicular cells or C cells of thyroid gland from CALC-1 gene present in 11 no. chromosome. Bacterial sepsis induces the expression of CALC-1 gene from extra thyroidal tissue which ultimately leads to release of procalcitonin.

Discussion:-

Many studies shows that PCT level elevates rapidly between 2-6 hours of bacterial infection and reaches to peak level within 6-24 hours (Angeletti et al., 2015). So PCT can be used for early detection and for reducing unnecessary antimicrobial therapy in sepsis suspected patient. Muller studies shows serum concentration of PCT, CRP, lactate, IL-6 all elevate accordingly during sepsis, septic shock or severe sepsis. They also conclude by analysing receiver operating characteristic (ROS) curve that among them PCT is the most trustable marker with almost 89% of sensitivity and 94% of specificity for diagnosis of sepsis (Jain et al., 2014). Also according to ACCP criteria based study among ICU patients PCT shows 72% of specificity and 76% of sensitivity and finally told that PCT is superior to CRP in terms of accuracy in identification of sepsis.

Conclusion:-

Thus PCT is the most reliable marker as it can differentiate between bacterial, non-bacterial and viral inflammation. Not only that it can be considered as most effective and valuable for early diagnosis as it posses high diagnostic accuracy. Further more studies are required for better understanding about its clinical application in early diagnosis and determining therapeutic approaches and also to declare it as a gold standard biomarker for septicaemia.

Abbreviation:-
ACCP= American College of Chest Physician
CALC= Calcitonin related C peptide
ICU= Intensive Care Unit
IL= Interleukin.
TNF= Tumor Necrosis Factor.

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