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Original Research Article

Bed side prognostic markers for dengue fever: serum lactate, base excess and central peripheral temperature gradient

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ABSTRACT

Background: Dengue is a common systemic viral infection, which has achieved epidemic proportion in India. The manifestations are varied, is most often a simple febrile illness, but at times it can be severe with hypovolemic shock resulting from excessive plasma leakage. Dengue shock syndrome is potentially fatal, with mortality ranging from <1% to 10%. The key to a good clinical outcome is understanding and being alert to the clinical problems that arise during the different phases of the disease, leading to a rational approach in case management. Investigations which can help in prognostication if used sequentially can be very effective in management. Serum lactate, base excess and central peripheral temperature gradient are few such markers which can help in identifying at risk patients.
Methods: In this study children in the age group of 6 months to 18 years, admitted in School of Medical Sciences and Research with complains of fever and found to be positive for dengue as per Ag/serology study were included. The study was done over a period of one year from August 2015 to August 2016. ABG/VBG for Serum lactate and base excess was done in all patients on confirmation of diagnosis of dengue and on progression of disease. Also, central and peripheral temperatures were measured.
Results: A total of 524 patients were enrolled. 77.29% were of dengue fever. 14.50% of dengue hemorrhagic fever and 8.21% were of dengue shock syndrome. Mean central and peripheral temperature difference was found to be higher for patients with DSS than with DHF and DF. High Lactate levels was found to be 100% sensitive and specific for mortality, likewise decreasing base excess was found to be 84.62% sensitive and 90.56% specific for mortality. Cp-T difference had sensitivity of 100% and specificity of 96.59%. All three had p-value of 0.01 which is significant.
Conclusions: A single ABG/VBG analysis can give values for Serum lactate and base excess both of which are very good indicators of intravascular fluid status and are easily available. Done sequentially, these tests can predict progression of dengue fever. Likewise, temperature gradient is not so expensive tool. Used properly, is very effective monitoring method.

Keywords: Central peripheral temperature gradient, DSS, DHF, Greater Noida, Prognostic factors, Severe dengue fever

INTRODUCTION

Dengue is a common systemic viral infection that generates a considerable economic burden for healthcare systems in tropical and subtropical regions of the world. It is estimated that about 40% of the world's population is at risk.[1,2]

The manifestations are varied, is most often a simple febrile illness, but at times it can be severe with

hypovolemic shock resulting from excessive plasma leakage due to a transient increase in systemic vascular permeability, the dengue shock syndrome (DSS). DSS is a potentially fatal, with mortality ranging from <1% to 10%.[3-6]

For a disease that is complex in its manifestations, management is relatively simple, inexpensive and very effective in saving lives, so long as correct and timely interventions are instituted. The key to a good clinical outcome is understanding and being alert to the clinical problems that arise during the different phases of the disease, leading to a rational approach in case management. Triage and management decisions at the primary and secondary care levels (where patients are first seen and evaluated) are critical in determining the clinical outcome of dengue. A well-managed front-line response not only reduces the number of unnecessary hospital admissions but also saves the lives of dengue patients.[2]

Scoring systems are available based on epidemiological information and clinical sign and symptoms which might be useful in detecting dengue fever very early prior to lab results. Examples are Dengue Fever scoring system, PELOD, PRISM 3. Some scoring systems like DIC score, helps to diagnose DIC and to discriminate DF and DHF from other febrile illnesses.[7]

Some simple bedside measures and investigation like core-peripheral temperature gradient, and base excess and lactate levels in ABG/VBG can give an idea of patient's circulatory status at the time of initial contact and can be very useful. This study was done to see if the above parameters correlate with dengue severity or not.

Serum markers of metabolic acidosis may be measured as part of the critical care diagnostic plan to assess the severity of injury, determine treatment efficacy, and provide prognostic information. The most common of these markers include lactate, base excess (or base deficit), bicarbonate, and pH. Sepsis or trauma, volume depletion, blood loss, septic shock, and systemic inflammatory syndrome can alter lactate levels. Knowing these levels, particularly early in the patient's presentation, can provide valuable information to help guide patient assessment and treatment.

Landmark studies in this area support the use of serum lactate in both the diagnostic and treatment phases for septic shock.[8-10]

In the surviving sepsis campaign, it was seen that lactate levels are critical parameter indicating sepsis induced hypo perfusion.[11] They found that lactate levels ≥4 mmol/L are significant.

A decreased base excess is thought to represent the presence of unmeasured anions. In acute trauma cases, the primary unmeasured anion is assumed to be lactate.[4] Therefore, base excess usually is viewed as a surrogate marker for lactic acidosis.[12,13]

So, we took base excess levels also, which are available in any ABG/VBG recording as early marker of hypo perfusion. It has been proven in studies that either arterial or venous base excess can be used.[14]

Peripheral temperature can be measured with an electronic temperature probe taped to the lateral aspect of great toe of the limb not overtly ischemic. The foot is usually used in preference to the hand as studies have revealed that hand temperature values were sometimes higher than those recorded on the foot and the correlation between the temperature of the hands and feet was not consistent. If an intravenous infusion is present in a foot or leg, that limb is not used for temperature monitoring.[15]

There are various methods of core temperature measurement. These are rectal, oral and tympanic thermometry.

Rectal thermometry has traditionally been considered the gold standard for temperature measurement but some studies have revealed limitations of this method.[16,17] A drawback of rectal temperature is that it changes slowly in relation to changing core temperature, and it has been shown to stay elevated well after the patient's core temperature has begun to fall, and vice versa. Rectal readings are affected by the depth of a measurement, conditions affecting local blood flow and the presence of stool. Rectal perforation is a known complication and without proper sterilization techniques, rectal thermometry can spread infection.[18,19]

Tympanic thermometers measure the thermal radiation emitted from the TM and the ear canal, and have therefore been called infrared radiation emission detectors (IRED). Because the amount of thermal radiation emitted is in proportion to the membrane's temperature, IRED accurately estimates TM temperature.[20] The TM's blood supply is very similar in temperature and location to the blood bathing the hypothalamus, the site of the body's thermoregulatory center. So, it is an ideal location for core temperature estimation.[21,22] Crying, otitis media or earwax have not been shown to change tympanic readings significantly.

METHODS

In this study children in the age group of 6 months to18 years, admitted in School of Medical Sciences and Research with complains of fever and found to be positive for dengue as per Ag/serology study were included. The study was done over a period of one year from August 2015 to August 2016.

A total of 524 patients were enrolled. ABG/VBG for Serum lactate and base excess was done in all patients on confirmation of diagnosis of dengue and on progression

of disease. Also, central and peripheral temperatures were measured. Core temperature was measured using tympanic thermometer, and peripheral temperature was taken on the distal aspect of a limb that was not overtly ischemic (usually the great toe). Room temperature was kept constant throughout the monitoring.

Serum lactate >4, base excess <-10 and central peripheral temp gradient >3 were taken as significant.

RESULTS

In total 524 patients were analyzed, of which 77% had dengue fever only, 76 (14.50 %) of dengue hemorrhagic fever (DHF), and 43 (8.21%) were of dengue shock syndrome (DSS). Out of 524 patients, 26 (4.96%) expired.

Table 1: Number of patients in different groups.

Dengue Stage	n	%
DF	405	77.29
DHF	76	14.50
DSS	43	8.21
Total	524	100

In those with DSS, mean lactate levels were 20.79±4.53 while in patients with DHF it was 14.54±2.16. In patients with dengue fever without any complication, mean lactate levels were less than 7.54±2.84.

Table 2: Mean levels and P- values of lactate, base excess and temp difference in different patient groups.

	DF		DHF		DSS		p-value			
	mean	±sd	mean	±sd	mean	±sd	overall	DF vs DHF	DF vs DSS	DHF vs DSS
Lactate Levels	7.54	±2.84	14.54	±2.16	20.79	±4.53	<0.001	<0.001	<0.001	<0.001
B.E	-3.92	±4.26	-8.47	±2.69	-16.12	±5.61	<0.001	<0.001	<0.001	<0.001
Temp. difference	1.75	±0.79	2.98	±0.38	4.26	±0.66	<0.001	<0.001	<0.001	<0.001
Age (years)	6.85	±3.19	6.28	±3.06	7.47	±2.88	0.133	0.150	0.225	0.050

Table 3: Table showing final outcome of patients.

Outcome	n	%
Alive	498	95.04
Expired	26	4.96
Total	524	100

Mean base excess level was -16.12±5.61 in DSS, -8.4±2.69 in DHF and -3.92±4.26 in DF. Decreasing base excess values indicates deteriorating volume status.

With increasing severity of disease mean central and peripheral temperature difference increased. It was found to be higher for patients with DSS than with DHF and DF. In those with DSS it was 4.26±0.66, in DHF 2.98±0.38 and in DF 1.75±0.79.

In those patients who expired, mean lactate level was 23.42±4.02, mean base excess was -17.38±6.95, and core-peripheral temp gradient was 4.54°F±0.68.

Table 4: Mean and p- values of lactate, base excess, temp gradient and age in patients with different outcomes.

	Expired		Alive		p-value
	mean	±sd	mean	±sd	
Lactate levels	23.42	±4.02	8.92	±3.97	<0.001
B. E	-17.38	±6.95	-4.96	±4.64	<0.001
Temp. Difference	4.54	±0.68	2.01	±0.92	<0.001
Age (years)	7.23	±2.74	6.80	±3.17	0.496

Table 5: Sensitivity, specificity, PPV and NPV of different prognostic markers.

		Expired		Alive		p-value	Sensitivity	Specificity	PPV	NPV	Accuracy
		n	%	n	%						
Lactate Levels	<18.15	0	0	498	100	<0.001	100%	100%	100%	100%	100%
	≥18.15	26	100	0	0						
B.E	≤-9.95	22	84.62	47	9.44	<0.001	84.62%	90.56%	31.88%	99.12%	90.27%
	>-9.95	4	15.38	451	90.56						
Temp. Difference	<3.65	0	0	481	96.59	<0.001	100%	96.59%	60.47%	100%	96.76%
	≥3.65	26	100	17	3.41						

High lactate levels were found to be 100% sensitive and specific for mortality, likewise decreasing base excess was found to be 84.62% sensitive and 90.56% specific for mortality. Cp-T difference had sensitivity of 100% and specificity of 96.59%. All three had p-value of 0.01 which is significant.

For lactate levels both PPV and NPV was found to be high. For base excess and temperature gradient NPV is higher.

DISCUSSION

Prognosticating a case of dengue is a challenging and daunting task. A number of studies have used other factors for prognostication like hepatomegaly, hematocrit, SGOT and SGPT levels, level of viremia, endothelial and immunological biomarkers like MIP 1 beta and IFN-gamma, and echocardiography to asses intravascular volume status but these are not available in most of the health facilities in India.[23]

Lactate is an important marker of tissue hypo perfusion because in conditions of shock/hypotension anaerobic metabolism ensues and leads to production of excess of lactate which can be used as a marker. Normal level is below one mmol/L in both arterial and venous blood.[24]

It also appears that lactate screening may prove beneficial even in normotensive, hemodynamically stable patients. Shapiro et al, in a study with 1,278 patients with infection, demonstrated that increasing lactate levels were associated with increased mortality. Lactate levels less than 2.5 mmol/L were associated with a 4.9% mortality rate compared to patients with lactate levels ≥4mmol/L who had an in-hospital mortality of 28.4%. A lactate concentration ≥4 mmol/L was 36% (95% CI 27-45%) sensitive and 92% (95% CI 90-93%) specific for any death.[25]

Measurement of c-pT has been used clinically for many years. Its usefulness in adult patients has been disputed.[26-28] As most have some form of invasive monitoring of volume status, its use could be regarded as outdated and irrelevant, in children the usefulness of central peripheral temperature gradient has been proven in many studies. Also, as invasive monitoring to volume status is seldom available in resource poor settings, use of temp gradient in this section is practical, cheap, less time consuming and efficient.[29]

CONCLUSION

As seen in the study a single ABG/VBG analysis can give values for serum lactate and base excess both of which are very good indicators of intravascular fluid status and are easily available. Done sequentially, these tests can predict progression of dengue fever. Similarly, temperature gradient is not so expensive tool. Used properly, is very effective monitoring method, is noninvasive so easy to use, can be used by nursing staff as well and can help in prognostication. There are studies which have validated the use of temperature gradient and Serum lactate in prognostication but in this study, use of base excess, which is known to be a good indicator of global hypo perfusion and emerging metabolic acidosis, in addition adds objectivity to the findings.

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