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Trends in Bacterial Blood Culture Isolates and Resistance in Children in Two Microbiologic Eras from a Tertiary Health Facility in North East Nigeria

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Abstract

Introduction: Antimicrobial Resistance surveillance is predicated on blood culture as a priority clinical specimen in especially resource limited settings. Establishing trends in blood stream infections and resistance patterns can inform institutional and national policy on antimicrobial stewardship, surveillance, infection prevention and control. **Methodology:** Blood Culture isolates in children (0 - 18 years) by conventional method from 2008-2012 and Bactec Automated culture system from 2015-2020 were retrieved. Information analyzed included age, sex, month, and year and culture growth/identity of microorganisms and their sensitivity/resistance patterns. Clinical and Laboratory Standards Institute (CLSI) guideline for antibiotic susceptibility testing was used. **Results:** 20,540 children were admitted: 8964 (44.6%) and 11,630 (55.4%) in the Manual and Bactec blood culture era respectively. Blood cultures were done in 5271 in the manual culture era and 1077 in the Bactec culture era; of these cultures, 514 (9.7%) and 461 (42.8%) were positive for isolates in the respective era (p = 0.01). There were no statistically significant differences in trend between positive and negative blood cultures in males and females. Newborns, followed by children 1 - 5 years had more blood culture performed on them than other age categories. In general, there is no significant relationship in blood culture outcomes between the age categories and sex of the patients. The isolation of *Staph aureus*, *Citrobacter* and *Alkaligenes* increased two-fold with Bactec automated system. Resistance to the quinolones and the penicillin was high. Resistance trend to Genticin, an aminoglycoside was less than 40%. Resistance to Ceftazidime was high. **Conclusion:** Antimicrobial resistance surveillance is critical to reduce AMR related morbidity and mortality.

Keywords

Trend, Blood Culture Isolates, Children, Manual, Bactec, Resistance

1. Introduction

Blood culture is the gold standard for the diagnosis of Blood stream infections [1]. Accurate and reliable diagnosis of blood stream infections is a microbiologic task of utmost clinical significance [2]. Antimicrobial Resistance AMR surveillance is predicated on blood culture as a priority clinical specimen in especially resource limited settings [3]. There were an estimated 4.95 million deaths associated with bacterial AMR in 2019, including 1.27 million deaths attributable to bacterial AMR. At the regional level, it was estimated the all-age death rate attributable to resistance to be highest in western sub-Saharan Africa, at 27.3 deaths per 100,000 [4]. In Nigeria, a situation analysis of antimicrobial use [5] and a National Action Plan for AMR [6] prioritized the use of blood culture in diagnosing BSIs. Low- and middle-income countries especially sub-Saharan Africa face many challenges when implementing blood cultures, due to financial, logistical, and infrastructure-related constraints [7]. In these settings, the conventional/manual culture methods remain the dominant systems while the automated blood culture systems have become the standard in high-income countries (HICs), and are relatively expensive and not universally available for implementation in most LMICs where [7] [8] [9] implementing automated microbiologic systems is feasible [7] [10]. Several reports [11] [12] [13] in LMIC showed that these systems show better performance than manual systems in terms of yield, sensitivity and especially speed of growth and overall turnaround time. Blood cultures are still indispensable for the diagnosis of BSIs however currently available molecular methods based on *in situ* hybridization-based methods, DNA microarray-based hybridization technology; nucleic acid amplification-based methods and combined methods [14] are a distant prospect for LMICs.

Establishing trends in blood stream infections and resistance patterns can inform health care needs assessment, service provision planning, institutional and national policy on antimicrobial stewardship, surveillance, infection prevention and control [15]. In Nigeria, a nationally representative epidemiologic data on Blood Stream Infections and their antibiotic sensitivity and resistance patterns is lacking [16]. With the triad of Malaria, malnutrition HIV and other prevalent childhood conditions strongly associated with the prevalence of Blood stream infection in the region clinical microbiology laboratories require urgent strengthening in Sub-Saharan Africa [17]. In Nigeria, there is paucity of data on two contrasting microbiologic laboratory periods in transition. We therefore aimed to report blood stream infection and resistance trends in children in our health facility over two microbiologic eras of earlier manual/conventional blood culture and current Bactec automated blood culture methods.

1.1. Method

The Federal Teaching hospital Gombe (FTHG) is currently a 500-bed health facility [18] which started providing health service to the public in the year 2000. The Medical Microbiology Department fully transitioned to automated blood culture system in 2015 from the conventional/manual system which was used at inception.

1.2. Subjects

Blood Culture isolates in children (0 - 18 years) by conventional method from 2008-2012 and Bactec Automated culture system from 2015-2020 were retrieved. Information analyzed included, age, sex, month, and year and culture growth/identity of microorganisms. Blood samples for cultures from consecutive children's admissions between 2008-2012 and 2015-2020 with suspected blood stream infections or sepsis were obtained using the Hospital standard procedure.

The BD Bactec (R) [19] 9050 instrument which is designed for the rapid detection of microorganisms in clinical cultures of blood was used. The Blood sample to be tested was inoculated into the vial which was entered into the Bactec 9050 for incubation and periodic reading. Each vial contains a sensor which detects increases in carbon dioxide, produced by the growth of microorganisms. The sensor was monitored by the instrument every ten minutes for an increase in its fluorescence, which was proportional to the amount of carbon dioxide present. A positive reading indicates the presumptive presence of viable microorganisms in the vial which are subsequently sub cultured for identification and antibiotic susceptibility testing. Clinical and Laboratory Standards Institute (CLSI) guideline for antibiotic susceptibility testing was used. From 2021 Bactec FX40 was introduced in the microbiology unit to replace the Bactec 9050 equipment and Vitek II automated platform for identification and antimicrobial susceptibility testing (ID/AST) was introduced in 2022. Our laboratory did not participate in any external quality assurance scheme.

1.3. Data Analysis

Data were entered into the EPInfo version 3.5.1 software and analyzed. Automated and manual BC were compared in terms of proportion positive and recovery of different bacteria were calculated using chi and Fischer's exact test. A p-value below 0.05 was considered as statistically significant. Yearly Blood culture sampling/admission was derived by dividing the number of blood cultures by admissions in the year.

1.4. Ethical Approval

Approval for this study was received from the Ethical Research Committee of the Federal Teaching Hospital Gombe.

2. Results

In Table 1, 20,540 children were admitted; 8964 (44.6%) and 11630 (55.4%) in the Manual and Bactec blood culture era respectively. Blood cultures were done in 5271 in first era and 1077 in the second era. Of these cultures, 514 (9.7%) and 461 (42.8%) were positive for isolates respectively. (p = 0.01). Blood culture cost rose from N500 ($1.1) for Manual method to N5000 ($11.1) for Bactec culture and is currently N8500 ($18.8). Of the total children admitted 63% and 9.2% had blood culture in the first and second era respectively. Cumulative Blood sampling for culture was 0.6 per admission in the manual culture era and 0.09 per admission in the Bactec era.

Yearly BC declined sharply when the Bactec 9050BD was introduced in 2015 largely because of increased in the cost of blood culture to 10 times above manual era.

Figure 1(a) and Figure 1(b) show the yearly admission, yearly blood cultures and yearly blood culture rate amongst admitted children in the two eras. Yearly blood culture rate among children admitted in the Manual era varied between 86.2% in 2008 and 68.8% in 2012. In the Bactec era this rate was between 10% - 19.4%. Blood culture sampling per patient admission ranged from 0.5 and 0.7 in the manual era and 0.005 to 0.06 in the Bactec era. The cost of one Blood culture

Table 1. Blood culture era, sex and yield.

	Manual blood culture Era	Bactec blood culture Era	
Year	2008-2012	2016-2020	
Paediatric admissions	8964	11,630	
Cost in Naira/culture	N300-N500:00	N5000:00	
Blood cultures Performed	5721	1077	
Blood culture rate /Era	63%	9.2%	
Blood culture/admission	0.6	0.09	
Positive Blood cultures	541	461	p = 0.01
Negative Blood cultures	5207	616	
Percent Positive	9.7%	42.8%	
Males positive	293 (54.2%) p = 0.3	252 (54.6%)	p = 0.00
Females positive	248 (45.8%)	209 (45.4%)	
Males negative	2922 (56.4%)	462 (64.7%)	
Females negative	2258 (43.6%)	252 (35.3%)	

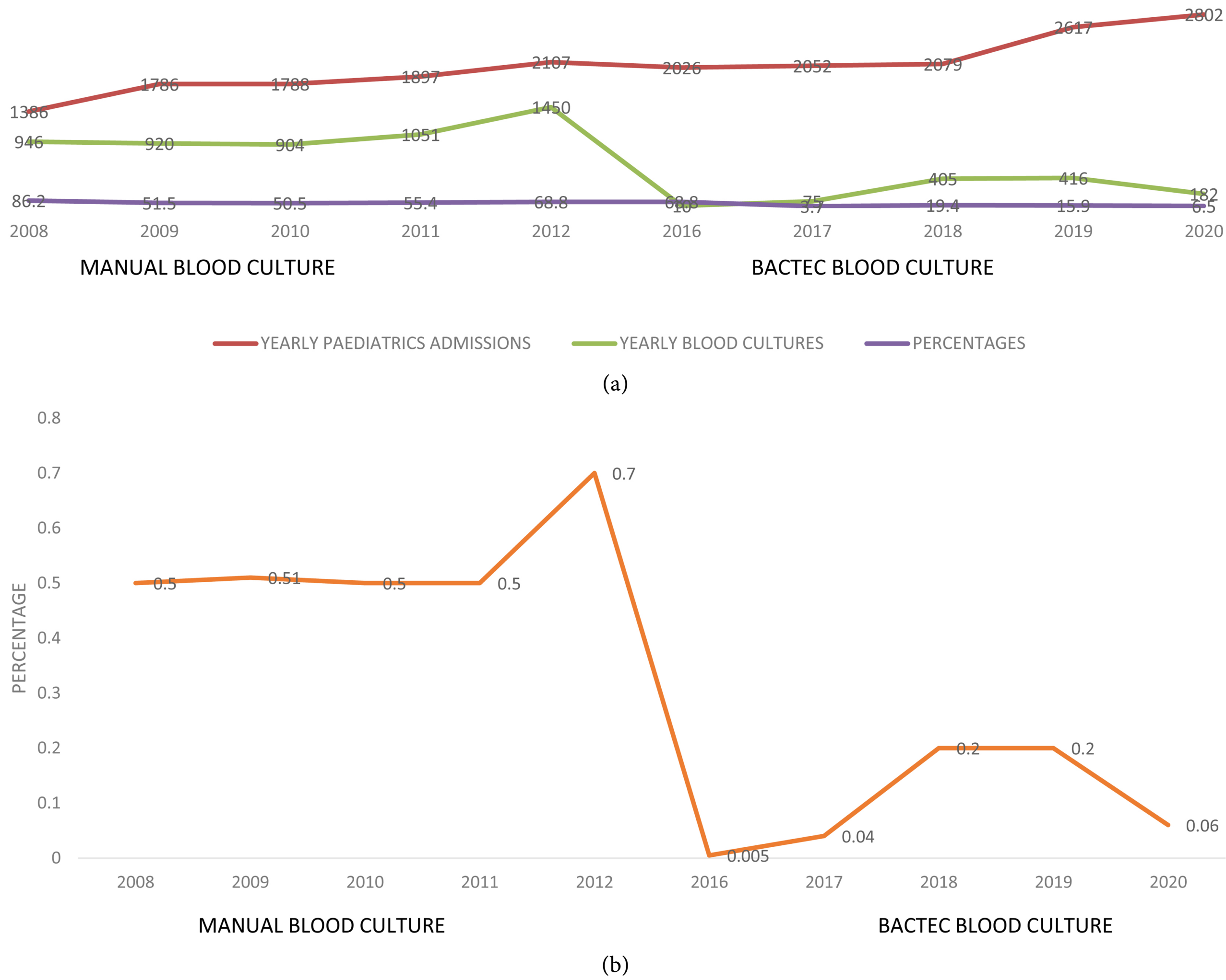

Figure 1. (a): Yearly trend in Blood culture rate per yearly patient admission in the two microbiologic eras in FTH Gombe Nigeria. (b): Yearly blood culture per patient admission in two microbiologic eras in FTH Gombe.

for Manual method was \$1.1 and \$11.1 (equivalent to the Nigerian currency, the Naira) in the Bactec era. The intervening years of 2013-2015 were not included as the numbers did not differ and two equal time intervals were used for this trend analysis.

In **Figure 2(a)** and **Figure 2(b)**, blood culture positivity rate peaked in 2008 and decreased to a lowest of 3.8% in 2010 in the manual blood culture era. In the Bactec era, peak positivity rate was 50% in 2016 with the lowest of 30.7% isolation rate.

In **Figure 3**, more males had received a blood culture than females on a yearly basis in both microbiologic eras but this was not statistically significant (x^2 = 13.173; p = 0.155). In both sexes blood culture declined with the advent of Bactec automated blood culture system, however there was no statistically significant differences in trend between positive and negative blood cultures in males and females (**Table 2**). In **Figure 4**, newborns, followed by children 1 - 5 years had more blood culture performed on them than other age categories. Adolescents

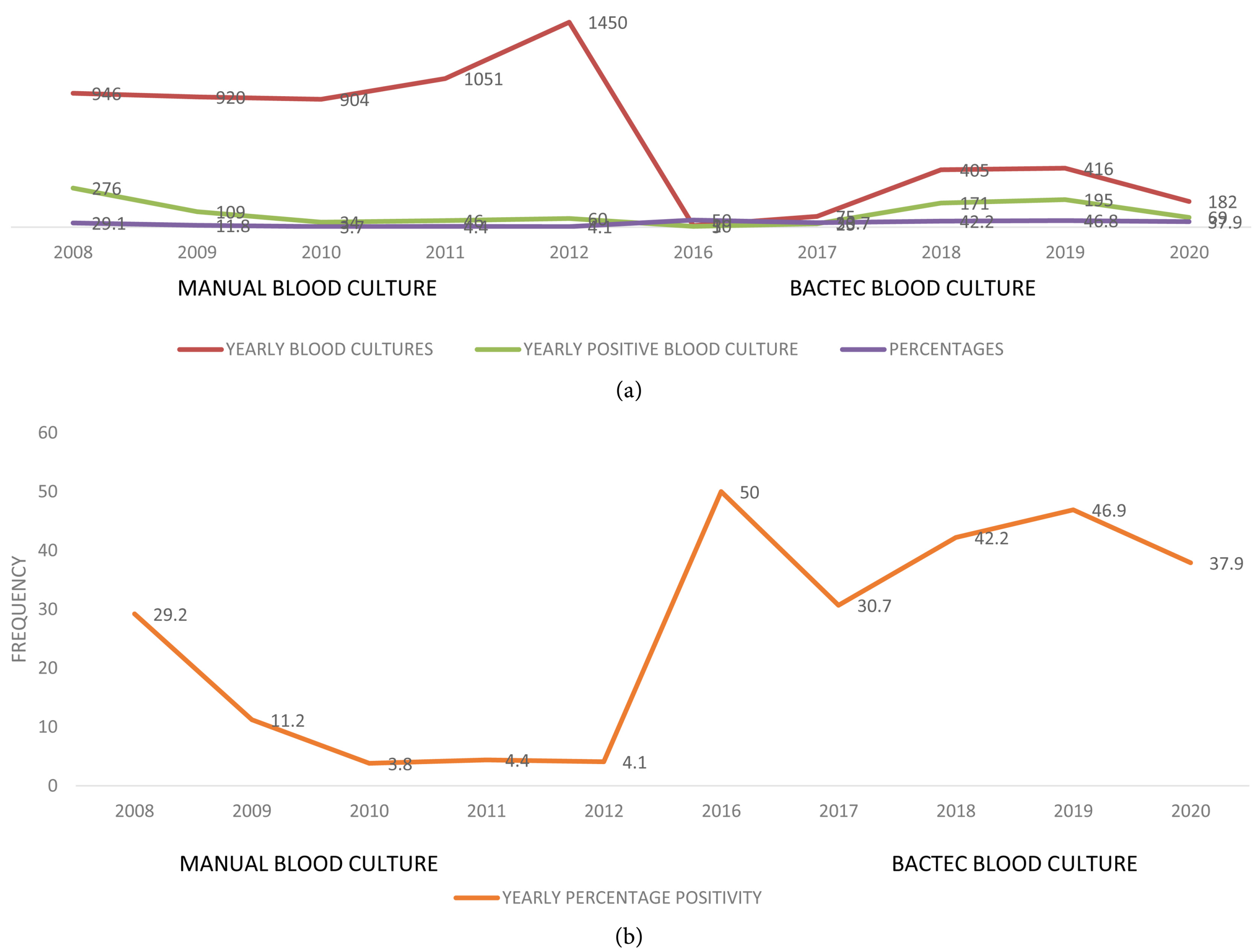

Figure 2. (a): Trend in Yearly blood culture percent positivity in two microbiologic eras in FTH Gombe Nigeria. (b): Trend in yearly blood culture positivity in children in the manual and Bactec era FTH Gombe.

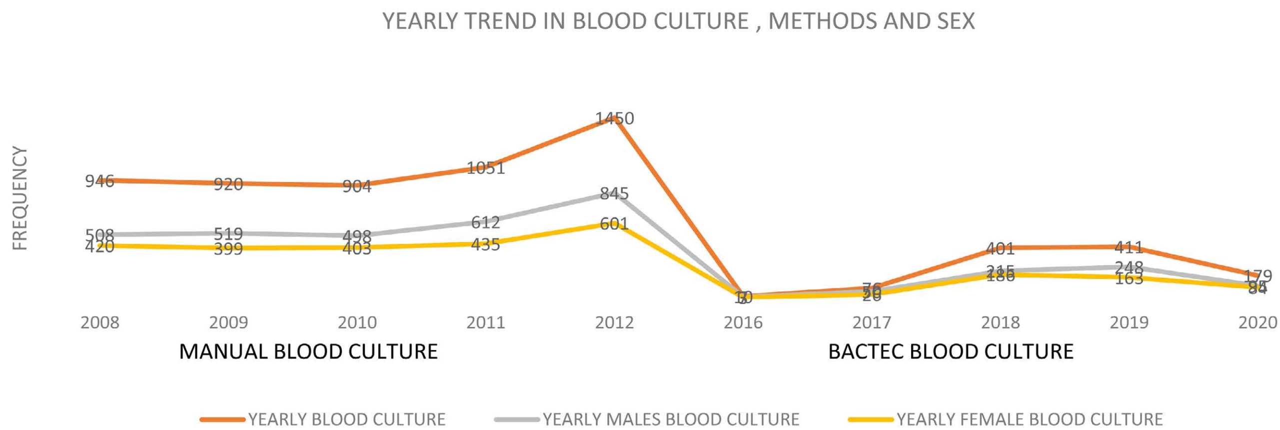

Figure 3. Trend in yearly blood cultures and Sex of Children admitted in the Manual and Bactec Culture eras in FTH Gombe (x^2 = 13.173; p = 0.155).

had the lowest rate of blood culture of all the ages. In all age categories, the culture rate declined with the use of Bactec automated culture method despite increasing child admissions. However, there was a statistically significant trend in

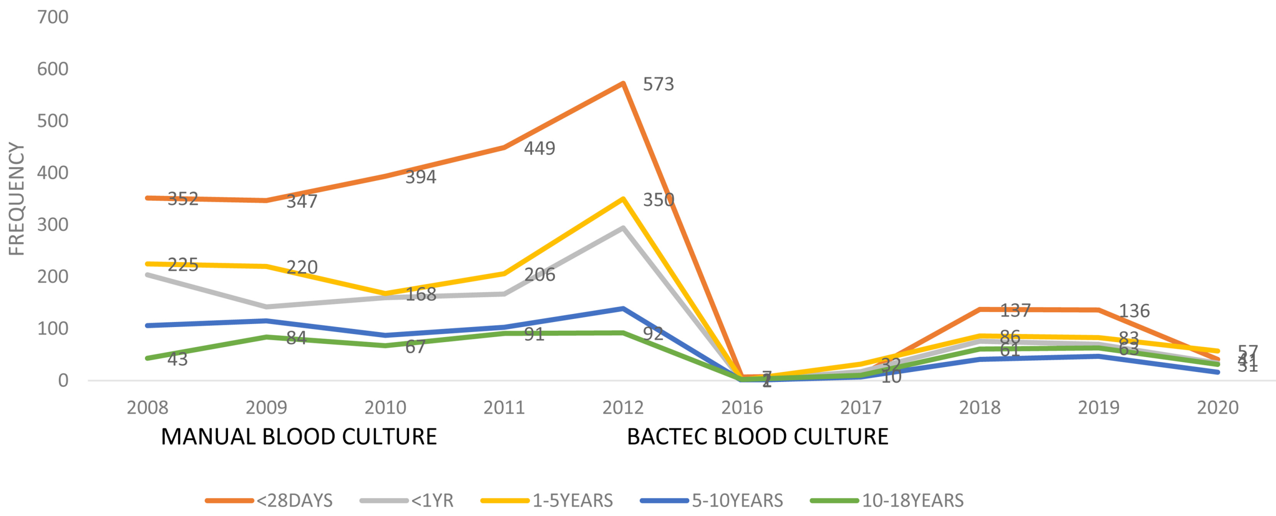

Figure 4. Trend in age group and yearly blood cultures in manual and Bactec blood culture era in FTH Gombe.

Table 2. Yearly trend of blood culture results and sex in two microbiologic eras in FTG Gombe.

	POSITIVE		NEGATIVE	
YEAR	MALES	FEMALES	MALES	FEMALES
2008	148	118	360	302
2009	60	48	459	351
2010	23	11	475	391
2011	31	15	581	420
2012	31	29	814	571
2016	3	2	4	1
2017	15	8	34	18
2018	92	78	121	108
2019	108	86	140	77
2020	34	35	61	49
Total	545	430	3049	2288
X^2, p-value	7.613, 0.574		15.014, 0.091	

blood culture results from the manual to the automated era (Table 3). In Table 4, there was in general no significant relationship in blood culture outcomes between the age categories and sex of the patients.

In Figure 5, of the priority pathogens, *Staphylococcus aureus*, *Klebsiella* and *E. coli* remain the most dominant especially in the manual era. The isolation of staph aureus increased two-fold with Bactec automated system. Citrobacter and alkaligenes isolation also increased about two-fold with the Bactec culture method.

In Figure 6, resistance to the quinolones and the penicillin in the early years was high ranging from 60% - 100% with sharp decline in 2016 and 2017 for ciprofloxacin, amoxyllin/clavulanate and amoxicillin as result of none testing. This

Table 3. Yearly trend in blood cultures results and age categories in two microbiologic eras in FTH Gombe.

	<28 days		28 days - 1 yr		1 - 5 yrs		5 - 10 yrs		10 - 18 yrs	
Year	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
2008	131	207	38	166	52	172	29	74	6	30
2009	58	287	14	128	20	200	7	108	6	78
2010	19	372	5	154	8	160	2	85	0	67
2011	28	420	6	161	7	197	4	101	1	89
2012	39	530	7	287	8	342	3	135	3	89
2016	5	2	0	0	0	1	0	0	0	0
2017	6	4	4	13	10	21	2	5	1	9
2018	72	65	24	51	40	46	15	26	19	41
2019	86	50	32	28	46	59	9	38	21	42
2020	22	19	10	24	21	36	8	8	8	23
Total	466	1956	140	1012	212	1234	79	580	65	468
X^2, p	515.528, 0.000		165.808, 0.000		250.230, 0.000		95.836, 0.000		85.143, 0.000	

was the year of the introduction of Bactec automated culture system with its tenfold increase in cost of blood culture. By the later years, resistance to these common antibiotics was less than 50% except for amoxycillin which showed a steep rise between 2018 and 2019 and decline in 2020. The difference in the number of bacterial isolates in the two eras may have accounted for the generally low resistance trend in the bactec era. Resistance trend to Genticin an aminoglycoside has remained less than 40% throughout the last ten years in our facility. At the start of the review resistance to Ceftazidime a 3rd generation cephalosporin was high at about 60% and remained so with substantial decline to 10% in the 2019 and 2020. The percentage of resistant bacterial isolates was arrived at using the multiple antibiotic resistance index [20] which represents number of antibiotics to which the test isolate depicted resistance divided by the number of antibiotics to which the test isolate has been evaluated for susceptibility in each year. The mean antibiotic resistance was derived from percentage resistance of each pathogen tested against each of the antibiotics in that year.

3. Discussion

In this study, there was a steady increase in paediatric admissions over the last decade in our facility. While this may be attributable to increasing child population and referrals [21], weak and ineffective primary health care especially and secondary health service have had their toll on tertiary healthcare service [22] [23].

Fever is common in Sub Saharan Africa and febrile illness remains a major cause of illness and death [24] [25]. With invasive bacterial infection contributing 10% - 13% of febrile illnesses [26] [27] blood culture and indeed pathogen

Table 4. Yearly trend in age group, sex and blood culture results in two microbiologic eras in FTH Gombe.

Age groups	<28 days		28 days - 1 year		1 - 5 years		5 - 10 years		10 - 18 years		x^2	p-value
Sex	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative		
2008												
Males	71 (54.2)	94 (45.4)	19 (50.0)	90 (54.2)	33 (63.5)	110 (63.9)	15 (51.7)	38 (51.4)	7 (53.8)	17 (56.7)	15.486	0.078
Females	60 (45.8)	113 (54.5)	19 (50.0)	76 (45.7)	19 (36.5)	62 (36.1)	14 (48.3)	36 (48.6)	64 (6.2)	13 (43.3)		
2009												
Males	27 (46.6)	157 (54.7)	10 (71.4)	84 (65.6)	15 (75.0)	112 (56.0)	4 (57.1)	54 (50.0)	2 (33.3)	45 (57.7)	14.305	0.112
Females	31 (53.4)	130 (45.3)	4 (28.6)	44 (34.4)	5 (25.0)	88 (44.0)	3 (42.9)	54 (50.0)	4 (66.7)	33 (42.3)		
2010												
Males	12 (63.2)	185 (49.7)	4 (80.0)	89 (57.8)	5 (62.5)	98 (61.3)	2 (100.0)	49 (57.6)	0	35 (52.2)	11.217	0.19
Females	7 (36.8)	187 (50.3)	1 (20.0)	65 (42.2)	3 (37.5)	62 (38.7)	0	36 (42.4)	0	32 (47.8)		
2011												
Males	16 (57.1)	242 (57.6)	6 (100.0)	97 (60.2)	5 (71.4)	116 (58.9)	2 (100.0)	59 (58.4)	1 (100)	56 (63.0)	7.739	0.561
Females	12 (42.9)	178 (42.4)	0	64 (39.8)	2 (28.6)	81 (41.1)	0	42 (41.6)	0	33 (37.0)		
2012												
Males	17 (43.6)	283 (53.4)	3 (42.9)	171 (59.6)	7 (87.5)	220 (64.3)	1 (33.3)	80 (59.3)	3 (100)	60 (60.6)	23.522	0.005
Females	22 (56.4)	247 (46.6)	4 (57.1)	116 (40.4)	1 (12.5)	122 (35.7)	2 (66.6)	55 (40.7)	0	29 (39.4)		
2016												
Males	3 (60.0)	2 (100)	0	0	0	1 (100)	0	0	0	1 (50.0)	1.905	0.592
Females	2 (40.0)	0	0	0	0	0	0	0	0	1 (50.0)		
2017												
Males	3 (50.0)	4 (100)	2 (50.0)	8 (61.5)	8 (80.0)	13 (61.9)	2 (100)	5 (100)	0	4 (44.4)	11.635	0.235
Females	3 (50.0)	0	2 (50.0)	5 (38.5)	2 (20.0)	8 (38.1)	0	0	1 (100)	5 (55.5)		
2018												
Males	36 (50.0)	34 (52.3)	15 (62.5)	31 (60.8)	23 (57.5)	25 (54.3)	8 (53.3)	14 (53.8)	10 (52.6)	17 (41.5)	4.923	0.841
Females	36 (50.0)	31 (47.7)	9 (37.5)	20 (39.2)	17 (42.5)	21 (45.7)	7 (46.7)	12 (46.2)	9 (47.4)	24 (58.5)		
2019												
Males	46 (53.5)	30 (60.0)	20 (62.5)	17 (60.7)	21 (45.6)	39 (66.1)	7 (77.7)	28 (73.7)	14 (66.6)	26 (61.9)	11.084	0.27
Females	40 (46.5)	20 (40.0)	12 (37.5)	11 (39.3)	25 (54.4)	20 (33.9)	2 (22.2)	10 (26.3)	7 (33.3)	16 (38.1)		
2020												
Males	10 (45.5)	9 (47.4)	4 (40.0)	19 (79.2)	13 (62.0)	20 (55.6)	2 (25.0)	2 (25.0)	5 (62.5)	11 (47.8)	14.358	0.11
Females	12 (54.5)	10 (52.6)	6 (60.0)	5 (20.8)	8 (38.0)	16 (44.4)	6 (75.0)	6 (75.0)	3 (37.5)	12 (52.2)		
	664.041, 0.000		205.256, 0.000		279.671, 0.000		93.392, 0.000		254,920, 0.000			

identification become critical elements of patient care and clinical microbiology in resource limited settings like sub-Saharan Africa [7] [28].

In this study, half to two thirds of children admitted during the Manual Blood culture era received a blood culture sampling indicating a substantial risk for blood stream infection. This is in contrast to the automated culture era where only a fifth of the children had blood culture sampled despite increasing patient admissions and risk for bacterial infection. The tenfold increase in the

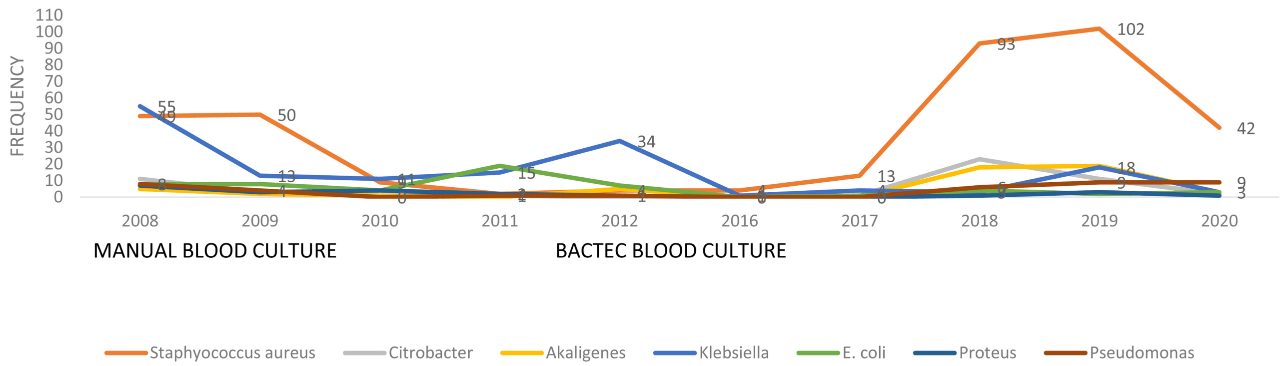

Figure 5. AMR priority and non-priority blood culture isolates in children in two microbiologic eras in FTH Gombe.

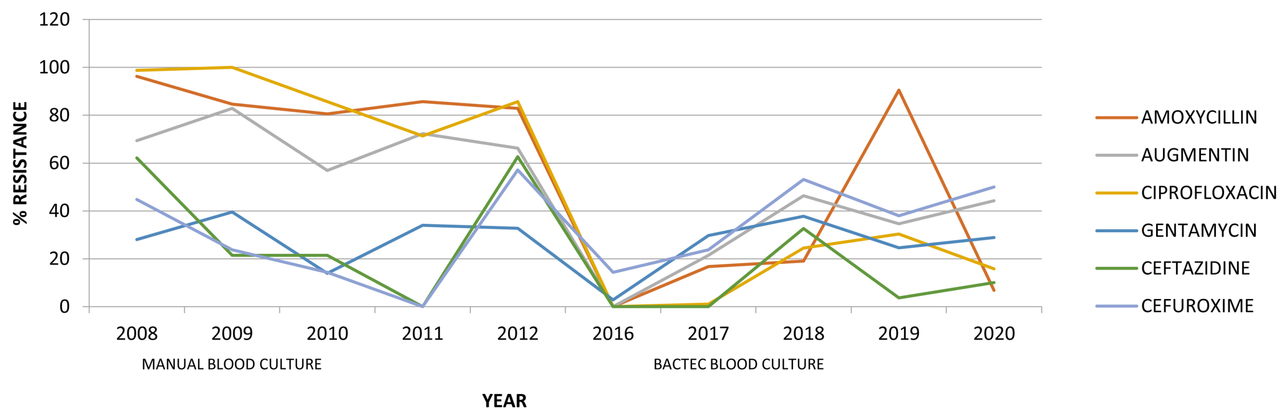

Figure 6. Trend in mean multiple antibiotic resistance index of priority and non-priority isolates in two microbiologic times in FTH Gombe.

break-even cost of Bactec blood culture had significantly negative impact on blood culture uptake in our facility. Blood culture per patient admission [29] [30] declined substantially during the Bactec era undermining the public health significance of etiologic diagnosis of acute febrile illness in a setting where clinical malaria is over-diagnosed, non-prescription antibiotics are prevalent and empiric prescription antibiotic by physicians is the standard clinical practice [16]. There is paucity of reports on the impact of automated microbiology methods on service uptake in Nigeria and in the sub-region. In Nigeria Health Insurance coverage is abysmally low at < 5% [31] with significant impact on out-of-pocket expenses in our subregion, North East of Nigeria, where Multidimensional poverty level is 90% and in Gombe state where child multidimensional poverty level is 95% [32]. These automated systems are costly, require regular maintenance and are not adapted to tropical, dusty environments, transferring costs to patients impeding the sustainable implementation of this technique in many developing countries [7] [33]. If according to a market forecasting study, manual blood culture systems will make up roughly two-thirds of the global blood culture market by 2025 [9] recommendations for improvement in manual blood culture and clinical laboratory methods in low resource settings require urgency of implementation [7] [34] [35].

Pathogen detection and identification is at the heart of tackling infectious diseases in general, whether it is for guiding optimal treatment or for detecting and controlling outbreaks of emerging and drug-resistant pathogens and good quality microbiological diagnostics remains the key factor [36].

Blood culture positivity trend was higher and sustained in the Bactec era compared to the Manual era. Previous reports in Nigeria [11] [37] [38] [39] and elsewhere [12] [13] [40] have shown higher pathogen yield and shorter turnaround time with Bactec culture systems over the conventional/manual method. However, and in general, access to quality-assured laboratory diagnosis has been a challenge in low-income and middle-income countries (LMICs) resulting in delayed or inaccurate diagnosis and ineffective treatment with consequences for patient safety [41] [42].

More male than female children had received blood culture on a year-by-year basis implying a substantial risk for blood stream infection among male children. But this was not statistically significant (x^2 = 13.173, 0.155). Similar findings were reported from Nigeria [43], Ghana [44], Tanzania [45] and Switzerland [46]. Most epidemiological studies have shown that being a male is a risk factor for infectious diseases and women are at less risk than men when it comes to developing most infectious diseases (x^2 = 7.112; 0.626) [47]. This sex dimorphism to infection is related to the interplay of age, comorbidities, genetic predispositions, geographical distribution of pathogens, health behaviors, access to healthcare, and hormonal influences [48] [49].

Throughout the review period newborns in particular and children under Five years had more blood cultures performed on yearly basis compared to other child age categories. The incidence of bloodstream infections is highest at extremes of age, in neonates and elderly people [50] and febrile illness is the commonest cause of hospitalization in children < 5 years in sub-Saharan Africa with bacterial bloodstream infections and malaria as major causes of death [24] [51] Several studies have documented risk factors for blood stream infection in the newborn and under 5 children [45] [52] [53]. Co morbidities like undernutrition, Malaria, anaemia and HIV have added to the burden of BSI in sub-Saharan Africa [16] [54] [55] [56].

In this study a trend towards *Staph aureus*, *Klebsiella and E. coli* being the dominant pathogens isolated from blood cultures of children during the manual era with variable frequencies was observed. *Staph aureus* isolation increased substantially in our centre with Bactec automated system. Similarly, Citrobacter and *alkaligenes* were isolated with increasing frequency in the automated blood culture system. While there is paucity of comparable reports to ours in the country and subregion early [57]-[63] and recent studies [43] [64]-[69], in Nigeria and elsewhere [30] [70] [71] [72] [73] have demonstrated the preponderance of *staph aureus*, *E. coli*, *Klebsiella and or Pseudomonas* in blood stream infections in children 0 - 18 years. While *Salmonella* and *Streptococcus pneumonia* were infrequently isolated in our study and others in Nigeria [57] [58] [64] [68] [69] [74] [75], the reports of Obaro *et al.* [16] and others in the country [76] [77] have demonstrated the significance of these pathogens in blood stream infections in children. Typhoid fever and Invasive Non Typhoidal *Salmonella* disease are major agents of invasive bloodstream infections in urban and rural locations, affecting children more commonly than adults across sub-Saharan Africa [78]. *Streptococcus pneumoniae* is capable of causing a spectrum of disease in children, the most severe of which is invasive pneumococcal disease (IPD), which includes bacteraemic pneumonia, meningitis and sepsis [75] Nevertheless, rates of pneumococcal disease are estimated to be highest on the African continent, causing over 4 million cases a year in children under 5 years; Pneumococcal disease also contributes to substantial mortality, driven predominantly by mortality from pneumococcal pneumonia [79]. With increasing pneumococcal vaccine coverage among children in sub-Saharan Africa, the burden of pneumococcal disease and its invasive forms is reducing [80] [81] [82]. The year-on-year isolation of *Citrobacter* and *alkaligenes* increased in the Bactec era compared to the manual blood culture period. *Citrobacter*, a facultative gram-negative anaerobic bacillus belonging to the family Enterobacteriaceae is being increasingly recognized to cause a wide spectrum of infections especially in immunocompromised or patients with comorbidities [83] [84] [85].

These gram-negative bacilli constituted 1.3% [86], 1.9% [87] of blood cultures isolates in Nigeria studies; 9.5% in Tanzania [88]; <1% in Malawi [89] and 2.2% in Rwanda [90], 2.4% in India [91], 1.2% in Kenya [92] and 15% in Ghana [72].

Alcaligenes spp are Gram-negative, obligate aerobic, oxidase-positive, catalase-positive, and nonfermenting bacteria. It is a potentially emerging pathogen and usually causes opportunistic infections in humans. The most commonly reported cases involved bacteremia, and most cases occurred in newborns and infants [93]. They are commonly found in hospital settings, such as in respirators, hemodialysis systems, and intravenous solutions [94]. A systematic review on bacterial isolates in sub-Saharan Africa by Reddy *et al.* [95] showed a <1% prevalence of *Alcaligenes*; recent systemic review in Africa and Asia [96] showed similar very low isolation rate. However, rather than a contaminant, *Alcaligenes* should be regarded as a pathogen, because global cases of life-threatening infections caused by *A. faecalis* are emerging [97]. The lack of widespread access to automated blood culture and pathogen identification systems in many developing countries may have contributed to the low isolation of some pathogens [16]. These automated platforms have improved time to detection and recovery of both aerobic and anaerobic organisms and made possible the neutralization of several anti-biotics present in blood culture media. They have minimized contamination and bio-hazard risk [10] [11] [16] [98].

In general, the unregulated [99] and widespread use of prehospital antibiotics [100] [101], empirical antibiotic prescription [102] [103] glaring gaps and constraints in clinical microbiology laboratory standards in especially sub-Saharan Africa [34] [104] have impacted significantly on pathogen isolation, identification and therefore surveillance. On the other hand, these aforementioned factors should give impetus an d accelerate policy revision, guideline development and update, on antimicrobials and clinical laboratory standards particularly now and within the arm bit of one health in sub Saharan Africa and other LMICs.

Antimicrobial resistance is a global threat and Africa bears disproportionately this burden [105] [106] [107]. Increasing cost of health care and poor patient outcomes are attributable to AMR especially in LMIC [108]. There is paucity of comparable resistance trend report in Nigeria and the subregion, however an earlier systematic review in patients with BSI in West Africa by Barnabe *et al.* [109] reported a 17.7% resistance to third-generation cephalosporin, 37.2% to Genticin, 68.4% to Ampicillin and 13.2% to ciprofloxacin. While resistance to 3 GC, Genticin and Ampicillin are comparable to the study mean values, ciprofloxacin resistance was threefold higher. This overall moderate level of AMR is likely to undermine typical empirical antibiotic strategy [109].

WHO recommends a third-generation cephalosporin as second-line antibiotic [110] but many low- and middle-income countries (LMIC) utilize third-generation cephalosporins-ceftriaxone as first-line treatment for severe sepsis at district, regional and tertiary health care facilities owing their widespread availability [77] [111] [112].

Lester *et al.* [113] in systematic review in SSA showed a mean estimate of 3 CG resistance to *E. coli*, *Klebsiella and Salmonella* of 18.4%, 54.4% and 1.9% respectively establishing significant heterogeneity not explained by differences in African region group of patients recommending that detailed clinical and demographic parameters should be collected to deepen the understanding of drug resistance isolates and the drivers of transmission of AMR pathogens [113].

Several Systematic reviews in children in Africa and other LMICS have reported varying 3 GC resistance of 19% against ceftazidime [114], 49% [115] and 33.9% to ceftriaxone [116]. These reviews also reported ciprofloxacin (43.3%, 44%, 12%), aminoglycoside (14%, 33.5%, 37.2%) and ampicillin (85%, 59.7% 68.8%) resistance rates, noting the high variation between antimicrobial groups and rates, high variation in antibiotics tested against the isolates with significant heterogeneity and low comparability of studies [114] [115] [116]. These researchers highlighted a continent-wide increase in AMR reporting and in resistance and substantial challenges in diagnostic microbiological data quality. Priority strengthening of laboratory capacity, standardized testing and surveillance efforts, and reporting of AST results are required to improve AMR [105] [114] [116].

A recent review showed *Escherichia coli*, followed by *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, *and Pseudomonas aeruginosa* as six leading pathogens for deaths associated with AMR and the following One pathogen-drug combination, *methicillin resistant S. aureus*, third-generation cephalosporin-resistant *E. coli*, carbapenem-resistant *A. baumannii*, fluoroquinolone-resistant *E. coli*, carbapenem resistant *K. pneumoniae*, and third-generation cephalosporin-resistant *K. pneumoniae* related AMR deaths [4]. In conclusion, while Blood sampling for culture has decreased in our facility on account of higher cost of Bactec blood culture, however the isolation of pathogens through this platform has increased significantly overall. *Staph au-*

reus was the leading isolate with *Alcaligenes and Citrobacter* also being grown increasingly with the use of Bactec automated method. Bacterial Resistance to commonly used antibiotics was multiple, and in general moderate to high.

4. Conclusion

Blood sampling for culture per patient admission is low in the Bactec era. The trend in blood culture positivity is higher with Bactec automated culture system with *Staph*. *Aureus* the leading pathogen isolated in both microbiologic eras. *Citrobacter* and *Alcaligenes* were increasingly isolated with the automated culture system. The trend in Resistance to commonly used antibiotics was high with mild to moderate resistance to aminoglycoside and the third-generation cephalosporin.

Limitation of the Study

As a retrospective study, microbiology quality and standards in laboratory could not always be guaranteed despite presence of highly qualified personnel and significantly the lack of any external quality assurance of these procedures in our laboratory.

Recommendations

Establishment of the collaborative multi-site multi-level health facility surveillance microbiology laboratories with effective and coordinated governance structure in Nigeria and other sub-Saharan African countries.

Collaborative partnership to upscale human capacity and automated microbiologic systems for culture and pathogen identification in specifically high patient flow facilities and the country in general which may impact positively on costs.

Advocacy for reduction in the unit price and consumables of automated blood culture and identification systems.

Author Contribution

WEI, MM conceived of the study and study design. WEI developed the first manuscript draft, and critically reviewed all drafts of the manuscript. IJ and IM critically reviewed bacterial isolates and reviewed draft manuscript. AJD and CO conducted quantitative analysis and critically reviewed the final manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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