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# Pediatric infectious diseases admissions: Sex differences and seasonal variations

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## Abstract

**Objective**: This study set out to assess sex differences and seasonal variations in Pediatric Infectious Diseases (PID) admissions.

**Methods**: One year retrospective study of PID admissions was conducted among children aged one month to 15 years. Relevant information retrieved from patients' hospital records were dates of admission and discharge, age, sex, final PID diagnoses and outcome.

**Results:** Of 1,035 patients' records assessed, 603 (58.3%) were males and 432 (41.7%) females ($p<0.001$). Males in ages 1-12 and 13-59 months contributed largely to the gender difference. Over the 12 months period, PID admissions mean was 86.25±21.92, with rainy and dry seasons means of 92.57±20.7 and 77.4±20.9, respectively ($p<0.001$). Ages 13-19, 60-119 and ≥120 months had significantly higher admissions mean during the rainy season ($p<0.001$ in each group), while higher admissions occurred among ages 1-12months in dry season ($p<0.001$). Top six PID managed were malaria, gastroenteritis, pneumonia, septicemia, meningitis and typhoid, and males had higher incidence in all except for typhoid, with only malaria having significant difference ($p<0.001$). Malaria, septicemia and typhoid incidence were higher significantly during the rainy season, while gastroenteritis occurred more in the dry season. Overall fatality rate was 4.6%; females and males rates were 6.3% and 3.5%, respectively ($p=0.661$). Rainy and dry seasons mortality means were 5±1.77 and 2.6±0.8, respectively ($p<0.001$).

**Conclusion**: Male children were more vulnerable to PID, with significant higher malaria incidence among them than females. PID incidence and mortality were significantly higher during the rainy season than dry. Malaria and gastroenteritis occurred significantly in rainy and dry seasons, respectively.

**Keywords:** Pediatrics; Infectious diseases; Sex differences; Season.

## 1. Introduction

Variations in diseases epidemiology and outcomes may be influenced by many factors. Infectious diseases, in particular, have been observed to have gender and seasonal variations [1]. Insight into sex and seasonal differences in pediatric infectious diseases (PID) occurrences and outcomes are important for planning, prevention, care and counseling, and their consideration when planning healthcare delivery at hospital and community levels are valuable and rewarding.

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Higher male morbidity with higher female mortality had been reported among children [2-4]. In the literature, the differences in female to male ratio in PID morbidity and mortality have been attributed to better female immune response to infections and vaccinations [5]. However, inconsistencies have been noted to exist in these differences [6]. Sex differences in PID occurrences and outcomes could be infection specific [7, 8], and hence could be the major cause of the inconsistencies.

Cultural and biological factors may affect occurrence, outcomes and responses of children to infections. Male child preference in some societies might predispose the female child to infections and poor outcome due to late presentation [9]. Genetic factors and hormonal changes are the main biological factors that affect the way children respond to infections [10]. Sex differences in some infectious diseases vary with age, indicating the influence of differential levels of sex hormones throughout different stages of life [7].

Seasonal influence is one of the elements contributing to the etiological factors of community-based diseases, including childhood infections [11]. Seasonal occurrences of infectious diseases have been variously attributed to changes in atmospheric conditions [12]. The recognition of seasonality of disease occurrence is longstanding, but the mechanisms underlying it remain poorly understood [13]. Recently, it was suggested that deficiency of vitamin D in cold and wet season may be an important factor in the susceptibility to infectious diseases during this period [13]. Improved understanding of infectious diseases seasonality will therefore give insight into host-pathogen interactions, which will improve the accuracy of public health surveillance and forecasting systems [13]. Also, awareness of this variation can aid the physicians in the prevention and counseling of the patients [11], and for the hospital or health managers to be well prepared for each season.

PIDs are the most common causes of childhood hospital admissions in the tropics [4], and as such, all aspects observed to affect morbidity and outcomes need to be studied to improve healthcare delivery. To best of the authors' knowledge, there is paucity of data in literature that studied in details sex differences and seasonal variations as regarding PID in Nigeria, and even in other developing countries. Therefore, this study set out to study sex differences and seasonal variations among children admitted for PID in a hospital in Nigeria.

## 2. Material and methods

This is a one year (October 1, 2010 to September 30, 2011) hospital-based descriptive retrospective study of PID admissions at the Department of Pediatrics, State Specialist Hospital, Akure, Nigeria, and now University of Medical Sciences Teaching Hospital Complex, Akure, Nigeria. Due to too many disruptions of healthcare delivery services as a result of industrial actions by health workers, it became difficult to get a continuous and complete one year data of patients managed as at when the study was conceptualized. Hence, the choice of October 2010 to September 2011 was made when a complete and continuous one-year data was obtainable. A continuous one-year data was particularly imperative because of the seasonal variations.

The study population was children between ages one month to 15 years whose final diagnoses were infectious diseases. Necessary information about the patients was retrieved from the wards admissions and discharges records and patients' case-notes. Information retrieved were dates of admissions and discharges, date of birth, age, sex, final infectious diseases diagnoses and mortality outcome.

Dates of admission were used to classify the period of admission into rainy (April to October) and dry (November to March) seasons. Ages were classified into age groups. Ethical Committee of Ladoke Akintola University of Technology (LAUTECH) Teaching Hospital (LTH), Osogbo, Nigeria approved the study.

IBM SPSS Software Package version 21.0 (SPSS Inc, Chicago, IL, USA) was used to determine frequencies, means, median, and also used to construct cross-tabulation and do statistical analyses. Statistical analysis methods employed were student t test, non-parametric tests, Z-statistics and Chi-Square ($\chi^2$) test. Level of statistical significance was p-value <0.05.

## 3. Results and discussion

Infectious diseases admissions into pediatrics wards during the study period were 1,035 children, 432 (41.7%) females and 603 (58.3%) males, giving a female to male ratio of 1:1.4 (p<0.001). The significantly higher number of males' admissions for PID was largely contributed by ages 1-12 and 13-59 months, see Table 1. The patients ages ranged between one (1) to 168 months, with median, mode and mean (standard error [SE]) of 21, 12 and 36.8 (1.2), respectively. The mean (SE) age of the females and males were 38.4 (1.9) and 35.7 (1.5) months, respectively (p = 0.938). Table 1 shows the number of PID admissions among the age groups in relation to sex with no significant difference observed in the distribution pattern (p = 0.385).

**Table 1** Infectious diseases admissions pattern among age group in relation to sex

| Age group (months) | Sex | | | |
|---|---|---|---|---|
| | Female | Male | Total | Z score (p) |
| | N (%) | N (%) | N (%) | |
| 1 - 12 | 155 (24.5) | 210 (57.5) | 365 (100) | 6.29 (<0.001)* |
| 13 - 59 | 165 (38.9) | 259 (61.1) | 424 (100) | 4.46 (<0.001)* |
| 60 - 119 | 78 (44.8) | 96 (55.2) | 174 (100) | 1.05 (0.294) |
| ≥120 | 34 (47.2) | 38 (52.8) | 72 (100) | 0.47 (0.635) |
| Total | 432 (41.7) | 603 (58.3) | 1035 (100) | 5.27 (<0.001)* |

*Significant; $\chi^2$ =3.042 df =3 p = 0.385

Table 2 shows the number of PID admissions and percentages for each month during the study period, with a mean (±SD) of 86.35 (±21.9). Total number of admissions, percentages and means ±SD during the rainy season (April to October) were: 648, 62.6% and 92.6±20.7 respectively, and while during the dry season (November to March) were: 387, 37.4% and 77.4 ±20.9 respectively. When the two means (rainy and dry seasons) were compared, PID admissions was significantly higher in the rainy season than dry season (p<0.001). Furthermore, rainy season admission means of ages 13-19, 60-119 and ≥120 months were significantly higher than that of dry season (p = 0.001 in each age group). The converse is true in ages 1-12 month where the mean was significantly higher in dry season than rainy season (p = 0.001).

**Table 2** Frequency of infectious diseases admissions among children on monthly basis

| Months | Frequency | Percentage |
|---|---|---|
| January | 86 | 8.3 |
| February | 70 | 6.8 |
| March | 114 | 11.0 |
| April | 94 | 9.1 |
| May | 52 | 5.0 |
| June | 83 | 8.0 |
| July | 113 | 10.9 |
| August | 117 | 11.3 |
| September | 103 | 10.0 |
| October | 86 | 8.3 |
| November | 60 | 5.8 |
| December | 57 | 5.5 |
| Total | 1035 | 100.0 |

Table 3 compares the pattern of PID admissions among age groups in relation to season (p <0.001). The proportions of infectious diseases admissions in all age groups, except ages 1-12 months were higher in rainy season than dry.

**Table 3** Infectious diseases admissions pattern among age groups in relation to season

| Age group (Months) | Seasons | | | |
|---|---|---|---|---|
| | Rainy N (%) | Dry N (%) | Total N (%) | Z score (p-value) |
| 1 – 12 | 198 (30.5%) | 167 (43.2%) | 365 (35.2%) | 2.493 (0.013)* |
| 13 – 59 | 278 (42.9%) | 146 (37.7%) | 424 (41.0%) | 1.034 (0.301) |
| 60 – 119 | 123 (19.0%) | 51 (13.2%) | 174 (16.8%) | 0.9207 (0.357) |
| ≥120 | 49 (7.6%) | 23 (5.9%) | 72 (7.0%) | 0.2626 (0.793) |
| Total | 648 (100%) | 387(100%) | 1035 (100%) | |

*Significant; $\chi^2$=18.253 Df=3 p<0.001

Table 4 shows the top ten PID diagnosed in relation to genders. In all the ten diagnoses, except for typhoid, males' incidence was higher than females. However, only in malaria was a statistically significant difference observed. Further comparison among various age groups revealed no significant difference between males and females except for malaria which occurred significantly (p<0.001) among males in ages 13-59 months. Among female gender, typhoid incidence was significantly higher among older female children (60 - ≥120 months) than younger female children (1 - 59 months) (p = <0.001).

**Table 4** Infectious diseases diagnosed during the period of review in relation to gender

| Diagnoses | Gender n (%) | | | | Z-value (P- value) |
|---|---|---|---|---|---|
| | Female n (%) | Male n (%) | Total n (%) | Overall % | |
| Malaria | 205 (41.1) | 294 (58.9) | 499 (100) | 48.2 | 3.9144 (p<0.001)* |
| Gastroenteritis | 86 (43.9) | 110 (56.1) | 196 (100) | 18.9 | 1.5953 (p =0.09) |
| Pneumonia | 61 (43.0) | 81 (57.0) | 142 (100) | 13.7 | 1.1652 (p =0.099) |
| Septicemia | 16 (42.1) | 22 (57.9) | 38 (100) | 3.7 | 0.9621 (p =0.336) |
| Meningitis | 11 (36.7) | 19 (62.3) | 30 (100) | 2.9 | 1.3537 (p =0.176) |
| Typhoid | 15(55.6) | 12 (44.4) | 27 (100) | 2.6 | 0.5784 (p =0.563) |
| Bronchiolitis | 5 (35.7) | 9 (64.3) | 14 (100) | 1.4 | 1.0289 (p =0.304) |
| HIV infection | 5 (41.7) | 7 (58.3) | 12 (100) | 1.2 | 0.5672 (p =0.257) |
| Measles | 4 (33.3) | 8 (66.7) | 12 (100) | 1.2 | 1.0977 (p =0.272) |
| Cellulitis | 3 (27.3) | 8 (72.7) | 11 (100) | 1.1 | 1.3707 (p =0.171) |
| Other infectious diseases | 21 (38.9) | 33 (61.1) | 54 (100) | 5.2 | 1.5925 (p =0.111) |
| Total | 432 (41.7) | 603 (58.3) | 1035 (100) | 100 | 5.269 (p <0.001) * |

*The asterisked have statistically significant gender differences (p<0.05).

Table 5 compares the means of the total number of PID admissions for each of the top ten infectious diseases diagnoses in the rainy and dry seasons, as rainy season lasted longer (7months) than dry (5months). Malaria, septicemia and typhoid occurred more significantly in the rainy season, while the incidence of gastroenteritis was significantly higher in the dry season.

**Table 5** Means infectious diseases admissions in relation to season

| Diagnoses | Season | | | | | t-value (p-value) |
|---|---|---|---|---|---|---|
| | Rainy n (%) | Dry n (%) | Total n (%) | Rainy Mean (SD) | Dry Mean (SD) | |
| *Malaria | 355 (71.1) | 144 (28.9) | 499(100) | 50.71(11.04) | 28.8(11.87) | 19.651 (<0.001) |
| *Gastroenteritis | 90 (45.9) | 106 (54.1) | 196(100) | 12.86 (5.72) | 21.2 (6.71) | 9.272 (<0.001) |
| Pneumonia | 80 (56.3) | 62 (43.7) | 142 (100) | 11.43 (5.42) | 12.4 (5.24) | 1.073 (0.285) |
| *Septicemia | 28 (73.7) | 10 (26.3) | 38 (100) | 4 (2.51) | 2 (1.41) | 2.376 (0.023) |
| Meningitis | 13 (43.3) | 17 (56.7) | 30 (100) | 1.86 (0.99) | 3.4 (2.87) | 2.058 (0.052) |
| *Typhoid | 18 (66.7) | 9 (33.3) | 27 (100) | 2.57 (0.9) | 1.8 (0.75) | 2.206 (0.037) |
| Bronchiolitis | 9 (64.3) | 5 (35.7) | 14 (100) | 1.29 (1.16) | 1.0 (1.26) | 0.435 (0.671) |
| HIV infection | 10 (83.3) | 2 (16.7) | 12 (100) | 1.43 (1.5) | 0.4 (0.49) | 0.929 (0.375) |
| Measles | 7 (58.3) | 5 41.7) | 12 (100) | 1.0 (1.31) | 1.0 (1.55) | 0.0 (1.0) |
| Cellulitis | 7 (63.6) | 4 (36.4) | 11 (100) | 1.0 (0.76) | 0.8 (0.75) | 0.422 (0.683) |
| Other infectious diseases | 31 (57.4) | 23 (42.6) | 54 (100) | 4.43 (0.9) | 4.6 (1.5) | 0.519 (0.606) |
| *Total | 648 (62.6) | 387 (374) | 1035 (100) | 92.57(20.9) | 77.4 (20.9) | 11.366 (<0.001) |

*Statistically significant seasonal differences

Forty-eight (48, 4.6%) out of 1,035 patients admitted for PID during the review period died, giving monthly mean (SD) mortality of 4.0 ±1.87. The main infectious diseases in this series that accounted for most (81.3%) of these deaths were: malaria (17, 35.4%), septicaemia (8, 16.6%), pneumonia (7, 14.6%), typhoid (4, 8.3%) and HIV (3, 6.3%). Deaths among the females were 27 (6.3%) out of 432 patients, while 21 (3.5%) out of 603 male patients died (p = 0.661). Pattern of mortality among the age groups in relation to sex is shown in Table 6, and no significant difference observed in the emerged patterns.

**Table 6** Pattern of mortality among age groups in relation to sex

| Age group (months) | Gender | | |
|---|---|---|---|
| | Female N (%) | Male N (%) | Total N (%) |
| 1 -12 | 11 (40.8) | 9 (42.9) | 20 (41.7) |
| 13 - 59 | 8 (29.6) | 9 (42.9) | 17 (35.4) |
| 60 - 119 | 6 (22.2) | 2 (9.5) | 8 (16.7) |
| ≥120 | 2 (7.4) | 1 (4.7) | 3 (6.2) |
| Total | 27 (100) | 21 (100) | 48 (100) |

$\chi^2 = 1.8714$ Df = 3 p = 0.5995

The highest mortality rate (16.7%) was recorded in the month of July (peak of rainy season) and followed by 14.6% in the month of April (early part of rainy season). January through to March (during dry season) recorded lowest mortality rate (4.2% each). Figure 1 shows infectious diseases mortality rates for each month including the number of deaths. On the whole, 35 (72.9%) out of 48 deaths occurred during rainy season, while 13 (27.1%) in dry season. Rainy season had mean mortality of 5 ±1.77 compare to 2.6 ±0.80 in dry season. The difference was statistically significant (p <0.001).

The mean duration of hospital stay for females was 3.27 ±2.92 days while males had 3.23 ±2.72 days (p = 0.796), and were comparable. Likewise, there was no significant difference between the means of hospital stay during the rainy (3.23 ±2.77 days) and dry (3.27 ±2.87 days) seasons (p =0.828).

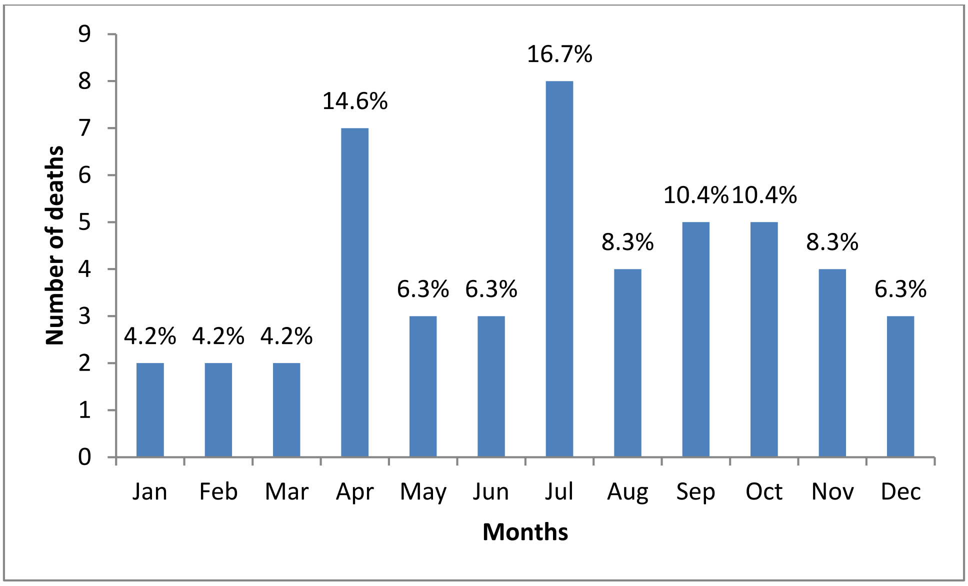


**Figure 1** The numbers and percentages of deaths due to infectious diseases in each month

In this series, the preponderance of male children admissions for infectious diseases was demonstrated and agrees with the findings in some studies [6-8]. However, similar reports have not been consistent for all infectious diseases [14, 15]. The inconsistencies in the reports of male predominance in PID occurrences could have resulted from the fact that different studies examined different infectious diseases. It has been mentioned that sex predilection in infectious diseases could be infection specific [7, 8], and could be the major cause of the inconsistencies.

Vulnerability of male children to infectious diseases are multifactorial, which could be behavioral [10, 14] (differences in exposure to common pathogens) and/or biological [10, 14, 16]. It has been documented that females mount stronger hormonal and cellular immune responses to infection or antigenic stimulation than do males [7, 17]. Even in infancy there is an intermittent surge of sex steroids referred to as mini-puberty, which could influence immune responses [7, 18]. Male sex hormone (testosterone) has been shown to have overall immunosuppressive effect reducing interferon (IFN) γ and interleukin 4 secretion in T cells [19]. On the other hand, estrogen potentiates the effects of T helper type 1 (Th1) cells and enhances Th1 cellular immune responses at lower doses, and increases T helper type 2 (Th2) cells responses and hormonal immunity at higher concentrations [7,20]. Females also have been observed to have more neutralizing antibodies than age-matched males [5, 21].

Interestingly out of the top ten infectious diseases in this series, only typhoid had higher incidence among females than males. Although the difference was not significant, this finding further alluded to the fact that sex difference in PID could be infection specific. Higher prevalence of typhoid infection among females in this study is contrary to some reports that showed a male predominance in typhoid incidence [22-24]. Authors have argued that male dominance in hospitalized patients with typhoid is not consistent [24], but varies with age group [22, 23].

On the overall in this study, infections occurred more significantly during rainy (cold and wet) season than dry, which was in agreement with the findings in some earlier studies [3, 22, 25]. Seasonal variations of infectious diseases have been variously attributed to changes in atmospheric conditions, the prevalence or virulence of the pathogen, or the behavior of the host [11, 12], which could be aggravated by global climatic change [13, 26]. Multiple climatic factors including temperature, humidity, rainfall, and wind speed have been implicated as contributing to increased infections during the cold and wet season [27]. Also implicated are increased indoor crowding and air pollution during cold months [26, 28], which sometimes come from wood-burning and stoves [27].

It has also been suggested that seasonal changes in vitamin D metabolism may be an important driver of cold and wet season susceptibility to infectious diseases [13, 29]. Diminished exposure to B-spectrum ultraviolet radiation in rainy season results in seasonal vitamin D deficiency thereby impairing host immune function [29]. Vitamin D plays an important role in phagocyte function regulation and is associated with the elaboration of antiviral and antibacterial peptides by immune cells [29].

The occurrence of more PID during cold and wet season could further be explained by the fact that environment being wet and cold increases pathogenic organisms' survival, environmental contamination and higher antimicrobial resistance [27, 30]. The third quarter (July-September) of the study year recorded the highest number of children admitted or died of infectious diseases. This is not surprising as the period fell within the peak of rainy season in the study area.

Diseases like malaria, pneumonia, septicemia and typhoid were prevalent in the rainy season because cold/high humidity affords the pathogens or vectors of these diseases ample opportunities to spread or breed. Mosquitoes in particular have more opportunity to breed and transmit malaria during rainy season than dry. And also, chilling environment affords micro-organisms to proliferate and contaminate food and sources of drinking water [31]. On the other hand, gastroenteritis and meningitis occurred more in the dry season, especially among infants. This also is not surprising as the common etiological agents of gastroenteritis among under-5 children are viral which are more prevalent during dry season [32]. Infants are usually more affected by enteric viruses causing gastroenteritis in the study environment [32], and this may be due to the fact that the infants are yet to develop immunity against common viral infections. The outbreak of meningitis normally occurs in dry season with its hot temperatures [33], aided by the dry and sandy harmattan that is conducive for the transmission bacterial meningitis [33].

Similar to what was earlier reported [34], proportion of death among females in this study was higher than males despite the latter having higher admissions, and the former are said to have better ability to handle infections [5]. Even though the difference was not significant but it deserves a closer attention. Could this phenomenon be as a result of the report that indicated that female children are often brought to health facilities in more advance stages of illness than boys or are taken to less qualified doctors when they are ill, and less money is spent on medicines for them than for the boys [3]? Or could it be due to environmental disadvantages for females, such as less adequate diet and health care [2]? Deaths patterns in both sexes in relation to age grouping were similar, but curiously older females succumbed to infections more than their male counterparts. Could this be as a result of the deleterious effect of an excessive Th2 response in females [34]? Researches are needed to be done in the study environment to answer these questions.

Mortality during the rainy season was observed to be significantly higher than dry season, similar to what previous studies had found [31, 35]. The reason for the higher mortality during rainy season is actually not known. However, a higher prevalence of infections during rainy season with the possibility of occurrence of more severe infections as result of a low level of body immunity may be contributing factors.

The average length of stay in hospital is often used as an indicator of efficiency, and it can be used to estimate the cost of care [36, 37]. In this series, the hospital stays of both males and females were equal, which is similar to finding in Qazvin hospitals [37], and could be inferred to mean that both genders incurred similar cost of care in infectious diseases management. Season had no effect on hospital stay. The reason for this finding is not readily available. However, relative higher mortalities during rainy season could have shortened the hospital stay during this period and made it comparable to that of dry season.

The limitation of this study stems from the fact that it is a retrospective study which has challenge of data loss. Some data could have been missed as a result of missing hospital records. Nevertheless, retrospective study in clinical settings is a gold mine especially in regard to medical audit, planning healthcare delivery and facility appraisal.

## 4. Conclusion

Male children are more vulnerable to infectious diseases. Infections incidence and mortality were significantly higher during rainy season than dry. Malaria was the commonest PID managed and occurred more significantly among males than females, and during rainy season than dry. Gastroenteritis occurred more significantly during dry season with the burden bore by infants.

Primary caregivers/guardians and health care providers should endeavor to put measures in place that would limit the exposure and vulnerability of children, especially the males, to infections, particularly during rainy season. Hospital/healthcare managers should make concerted efforts to plan and make human and material resources available to prevent and manage more PID during rainy season when there would be more children visiting health facilities because of infections.

## Compliance with ethical standards

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*Disclosure of conflict of interest*

The authors have no conflicts of interest to declare.

*Statement of informed consent*

Informed consent is not applicable because of the retrospective nature of the study.

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