



# Pediatric major burns: a monocentric retrospective review of etiology and outcomes (2008–2020)

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## Abstract

**Background** Burns are one of the most common causes of mortality and morbidity among children. This study aims to assess the epidemiology of pediatric major burns in a third level hospital in Spain to evaluate demographics, etiology, and outcomes.

**Methods** A retrospective study was held by the Plastic, Reconstructive and Burn Surgery department of the hospital. We included 147 patients under 18 admitted to hospital between January 2008 and December 2020 who meet the inclusion criteria: partial thickness burns > 10% total body surface area (TBSA) in patients < 18 years old. Clinical data extracted included age, gender, date of admission, %TBSA, burn types, severity and sites of burn, length of stay, length of ventilator support, intensive care admission, blood transfusion, surgical interventions, and complications.

**Results** Three groups of age were analyzed. The average %TBSA was 18.7 (SE 0.9). Scalds were the main mechanism of injury (70.1%) and upper extremity was the most frequent location affected (68%). The 28.6% of patients suffered some complication, but the mortality rate was low (0.7%). In our series, the group aged 13–18 showed significantly higher %TBSA, more number of surgeries and blood transfusions.

**Conclusions** Scald burns are the most frequent mechanism of injury in pediatric burns. However, teenagers suffer more severe burns and complications, usually caused by flame. Despite the low mortality rates, more measures of prevention should be taken to increase children security.

Level of evidence: Level IV, Risk/Prognostic.

**Keywords** Pediatric major burns · Etiology · Mortality · Outcomes

## Introduction

Burns are common causes of mortality and morbidity among children, especially in undeveloped countries [1, 2]. Moreover, burns are the third most common mechanism of accidental death in children between 5 and 9 years old [3] and

about 84,000 children under 14 needed medical treatment due to burn injury in USA in 2017 [4]. Several papers have reported that pediatric burn admissions, morbidity, and mortality have decreased during the last years in both USA [5, 6] and Australia [7]. An epidemiological study of mortality due to burn in 2018 in Spain assessed that the age-adjusted mortality rate (AMR) was 0.36 per 100,000 population in both genders, and particularly lower in people under 35 years old (AMR 0.10 per 100,000) [8].

Another recent study carried out in Spain, as a collaborative work between the Mapfre Foundation and the Spanish Association of Burns (AEQUE), collected relevant epidemiological data on burns in the period 2011–2017 [9]. The survey included 1050 patients between 0 and 14 years old that were admitted in all Burn Units in Spain (68% men and 32% female). Scalding was the main mechanism of burn ( $n = 714$ , 68%) with a mean of total body surface area

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(TBSA) of 7.8% and mean age of 2.8 years old. However, flame was the mechanism of injury in 315 patients (30%) with a mean TBSA of 8.1% (very similar to scalding), but greater mean age (9.1 years old).

Teenagers usually suffer flame burns due to experiment with fire, while scald burns more often occur in younger children [10, 11]. Some studies have described that the inhalation injury causes half of the deaths related to burn injury [10]. Although numerous studies about great burns have been reported, pediatric major burns are frequently excluded.

The primary evaluation of a pediatric burn includes measures of the extension, depth, and location of the burn [12, 13]. Although the rule of nines is a useful tool in adults, the Lund and Browder tables provide a better estimation of large TBSA for pediatric burns [14].

Some burn patients require multidisciplinary clinical approach and should be transferred to a Pediatric Burn Unit. These patients include children with any of the following traits: > 10% TBSA burns, third-degree burns, evidence of inhalation, electric or chemical burns, and face, feet, genitalia, or perineum burns. The calculated %TBSA by non-plastic surgeon is often overestimated in comparison to the posterior assessment at the burn unit [15].

To the best of our knowledge, our current study is the first in analyzing pediatric major burn patients in a single burn unit in Spain. Our University Hospital contains the main burn unit of the south of the country. In 2019, the Andalusian population under 18 was 1,593,204; with 554,983 children aged 0–6; 577,422 aged 7–12; and 460,799 aged 13–18 ([www.juntadeandalucia.es](http://www.juntadeandalucia.es)). The vast majority of previous studies in the literature included all pediatric burn admissions, but our team specifically wanted to focus on major burn patients. As a referral center, we have a children's hospital where patients are treated by pediatricians specialized in burns, especially by Intensive Care Unit professionals. The purpose of this study is to evaluate epidemiology and demographics data of pediatric major burns in a third level hospital, with the goal of identifying high risk groups and to establish prevention measures.

## Materials and methods

A retrospective study was held by the Plastic, Reconstructive and Burn Surgery department in a third level hospital in Spain. Anonymity was maintained during patient inclusion. Local ethics committee approved this project.

### Study design

Data for the current study were extracted from the database provided by the institution's burn department between

January 2008 and December 2020. Digital medical records were reviewed.

### Inclusion criteria

We included admitted patients under 18 years old with partial thickness burns greater than 10% TBSA according to the terms established by the American Burn Association Burn Center Referral Criteria [16].

### Exclusion criteria

We excluded patients over 18 years old, outpatients, and patients admitted for other reasons than thermal injury.

### Sample

A total of 251 pediatric burn patients were admitted during that period, but only 147 pediatric major burns fulfilled the inclusion criteria and were consequently analyzed. Clinical data extracted included age, gender, date of admission, percentage of TBSA (%TBSA), mechanism of burn injury (scald, flame, contact, chemical, and electrical), location of burn, length of stay (LOS), length of ventilator support, intensive care admission, surgical interventions, and complications. The revised Baux score ( $rBaux = \text{age} + TBSA\% + 17 \times \text{inhalation injury}$ ) was used to predict risk of mortality [17, 18]. Patients were divided into 3 groups based on age: 0–6 years old, 7–12 years old, and 13–18 years old.

Categorical variables were compared using the chi-squared test, and continuous variables were compared using analysis of variance, Student's *t*-tests, and ANOVA. Statistical significance was accepted at the level of  $p < 0.05$ . Microsoft Excel™ (2010) and SPSS Statistics (25) were used in this analysis.

## Results

A total of 106 patients were aged 0–6 years old (72.1%), 23 were 7–12 years (15.6%), and 18 were within the 13–18 years old age group (12.2%). A total of 91 (61.9%) were male and 56 (38.1%) were female (Table 1). The sex ratio was calculated (1.62). When we compare the different age groups, scald was significantly the most common mechanism of injury in children aged 0–6 (87.7%), whereas flame was the most frequent in children aged 7–12 (65.2%) and those aged 13–18 (66.7%),  $p < 0.01$ . The great majority of cases were accidental (98.6%), and only two cases of child abuse were detected (1.4%).

**Table 1** Demographic profile of 147 pediatric major burn patients, 2008–2020

	Male	Female	Total
<b>Age 0–6 years</b>			
Count	60	46	106
% within age group	56.6	43.4	100.0
<b>Age 7–12 years</b>			
Count	14	9	23
% within age group	60.9	39.1	100.0
<b>Age 13–18 years</b>			
Count	17	1	18
% within age group	94.4	6.6	100.0
<b>Total</b>			
Count	91	56	147
%	61.9	38.1	100.0

**Table 2** Mean percent TBSA burned according to etiology

Etiology of burn injury	Mean %TBSA (SE)	N	% of total sum
Flame	26.9 (2.5)	38	25.9
Scald	15.7 (0.7)	103	70.1
Electric	24.0 (14.0)	3	2.0
Chemical	15.0 (5.0)	3	2.0
Total	18.7 (0.6)	147	100.0

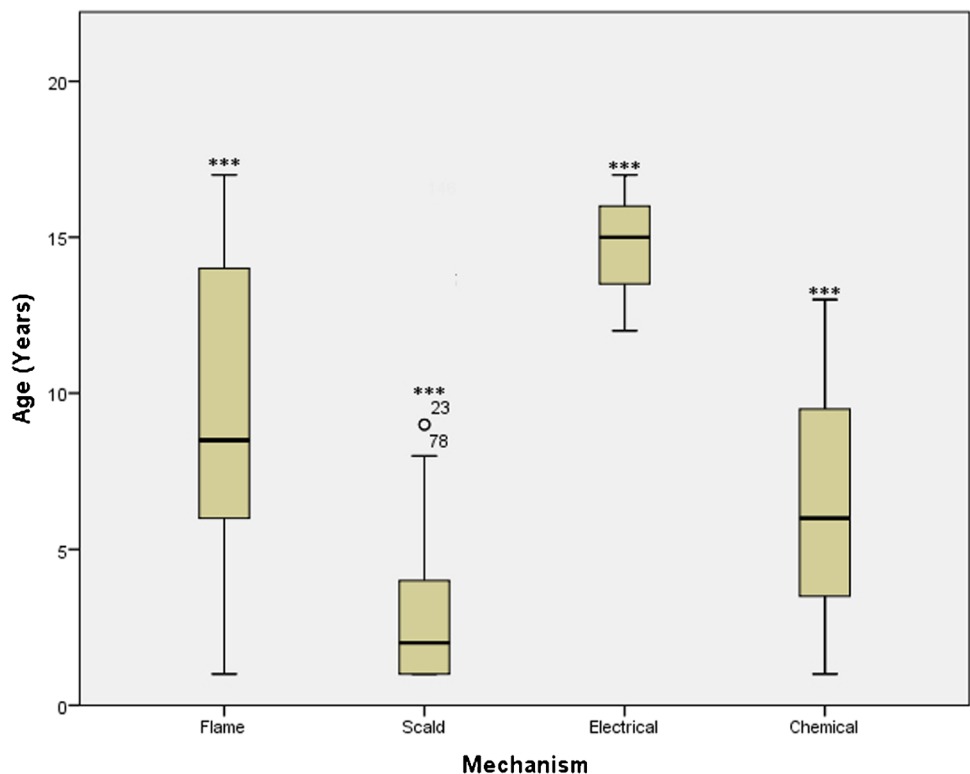
### Burn types

Scald burns constituted the majority of cases (70.1%) and were attributable to hot liquids related to cooking, including grease, milk, or soup. Flame burns comprised 25.9% of total burns, followed by electrical injuries in 2% and chemical burns in 2%. Among scalds, hot water was predominant in 50.3%, followed by grease in 12.9% and hot milk or soup in 6.8% (Table 2). A statistically significant difference was observed between age and burn mechanism. Thus, scalding was more frequent in young children, with a mean age of 3.0 years (SE 0.3), as compared to chemical burns (6.7 years, SE 3.5), flame (9.2 years, SE 0.8), and electrical causes (14.7 years, SE 1.5) (Fig. 1).

### Severity of burns

The total mean average of TBSA was 18.7% (SE 0.9), ranging from 10 to 66%. The mean TBSA percentage in female patients was 17.7% (SE 1.1) and the mean TBSA in males was 19.4% (SE 1.4). The mean TBSA at 0–6 years (16.8%, SE 0.85) was significantly smaller than at 7–12 years (23.1%, SE 3.1,  $p < 0.01$ ) and at 13–18 years (24.4%, SE 3.9,  $p < 0.01$ ). This parameter in flame burns was significantly greater than in scald burns (26.9%, SE 2.5 versus 15.7%, SE 0.7, respectively,  $p < 0.001$ ). Among scald burns, hot water had the largest TBSA (16.2%, SE

**Fig. 1** Box-and-whisker plot of age according to burn mechanism. \*\*\* $p < 0.001$



0.9), with no significant differences among other scald types. Mean TBSA of patients admitted at ICU was 30.9% (SE 2.7).

Seventy-three (49.7%) patients suffered partial-thickness burns and 74 (50.3%) resulted with full-thickness burns. Table 3 describes the thickness of burn registered according to the mechanism of injury. Children aged 7–12 ( $n = 16$ ) and 13–18 ( $n = 10$ ) showed greater full-thickness burns as compared to younger children ( $n = 48$ ), although not statistically significant.

### Burn sites

Analysis for anatomical location of burn injury and groups of age were also performed (Table 4). The results showed that upper extremity was the site most frequently burned (68.0%,  $n = 100$ ). Chest (61.9%,  $n = 91$ ) and head and neck (53.1%,  $n = 78$ ) were the next common locations of injury. The lower extremity injury was significantly greater in patients aged 13–18 than in other groups ( $p < 0.05$ ).

**Table 3** Thickness of burn registered according to the mechanism of injury

Mechanism ( $n$ )	Partial-thickness burn $n, \%$	Full-thickness burn $n, \%$
Flame (38)	8 (21.1%)	30 (78.9%)
Scald (103)	63 (61.2%)	40 (38.8%)
Hot water (74)	49 (66.2%)	25 (33.8%)
Grease (19)	7 (36.8%)	12 (63.2%)
Milk, soup (10)	7 (70.0%)	3 (30.3%)
Electric (3)	1 (33.3%)	2 (66.7%)
Chemical (3)	1 (33.3%)	2 (66.7%)
Total	73 (49.7%)	74 (50.3%)

**Table 4** Anatomic location of injury for 147 pediatric major burn patients, 2008–2020)

Anatomic location of burn injury $n, \%$	Total (147)	Age 0–6 years (106)	Age 7–12 years (23)	Age 13–18 years (18)
Head and neck	78 (53.1%)	56 (52.8%)	13 (56.5%)	9 (50.0%)
Upper extremity	100 (68.0)	76 (71.7%)	16 (69.6%)	8 (44.4%)
Hands	37 (25.2%)	23 (21.7%)	8 (34.8%)	6 (33.3%)
Lower extremity	79 (53.7%)	51 (48.1%)	13 (56.5%)	15 (83.3%)*
Feet	19 (12.9%)	12 (11.3%)	5 (21.7%)	2 (11.1%)
Genitalia	13 (8.8%)	10 (9.4%)	0 (0%)	3 (16.7%)
Chest	91 (61.9%)	69 (65.1%)	13 (56.5%)	9 (50.0%)
Abdomen	46 (31.3%)	31 (29.2%)	9 (39.1%)	6 (33.3%)
Back	32 (21.8%)	21 (19.8%)	8 (34.8%)	3 (16.7%)

\*  $p < 0.05$

### Resuscitation formula

To achieve fluid resuscitation, Galveston formula was the more often employed (83.7%,  $n = 123$ ), followed by Parkland formula (15.0%,  $n = 22$ ), and BET formula [19] (1.4%,  $n = 2$ ).

### Blood transfusions

Forty (27.2%) patients needed blood transfusions, with a mean of 8 (SE 1.8). Group  $> 20\%$  TBSA needed more blood transfusion in comparison to the group  $\leq 20\%$  TBSA (73 versus 11.8%,  $p < 0.001$ ). Significant differences are also observed between the 3 groups, with children aged 13–18 undergoing a mean blood transfusion of 4.6 (SE 2.7), followed by children aged 7–12 (4.43, SE 1.9) and children aged 0–6 (1.3, SE 0.5),  $p < 0.05$ .

### Frequency of surgery

Skin grafting was performed for 78 patients (53.2%) with a mean number of 2.1 operations (SE 1.8) and a range varying from 1 to 10. The mean number of surgeries was significantly lower in children 0–6 (0.9, SE 1.4) as compared to children 7–12 (1.9, SE 0.5) or children 13–18 (1.6, SE 0.5),  $p < 0.05$ . Different surgical techniques were employed: cadaveric allograft (4.1%,  $n = 6$ ), Biobrane® (Smith&Nephew, London, UK) (12.9%,  $n = 19$ ), Cultured Epithelial Autograft (2.7%,  $n = 4$ ), and amniotic membrane (2.7%,  $n = 4$ ). Furthermore, 15 patients (10.2%) required initial escharotomy due to signs of compartment syndrome. Also 10 patients (6.8%) included in the study needed secondary surgical interventions after discharge, without significant differences between groups of age.

## Hospitalization

Overall, mean LOS was 20.5 days (SE 2.3) for all patients, and 42.5 days (SE 8.1) for those admitted to the intensive care unit (range 6–267 days). Mean LOS in the group aged 0–6 was 18.7 days (SE 2.9) while in the groups aged 7–12 and 13–18, this value was 27.6 days (SE 4.8), and 22.4 days (SE 5.2) respectively, with no statistical differences.

## Complications and mortality

The 28.6% ( $n=42$ ) of patients suffered some complication. The 43.5% of patients ( $n=10$ ) aged 7–12 showed higher rates of complications compared with children 0–6 (24.5%,  $n=26$ ) or with patients aged 13–18 (33.3%,  $n=6$ ), not statistically significant. Catheter-related bloodstream infections were significantly greater in group aged 7–12 ( $n=4$ ,  $p<0.01$ ), whereas ventilator-associated pneumonia was significantly lower in the group aged 0–6 ( $n=5$ ,  $p<0.05$ ). The tract urinary infection in females showed significant differences with respect to males ( $n=8$  vs  $n=2$ ,  $p<0.01$ ).

When divided by TBSA, the complications in patients with  $>20\%$  TBSA were significantly greater than in patients with  $\leq 20\%$  TBSA (25 vs 17,  $p<0.001$ ). Table 5 describes each complication in both groups. ICU patients showed higher rates of complications (71.4% vs 28.6%,  $p<0.001$ ).

Only one pediatric patient died (0.7%), showing a TBSA of 62%. The rBaux score was calculated for all patients admitted and they were divided into two groups that included those with rBaux scores lower than 75 ( $n=144$ ) and those with scores ranging from 75 to 97 ( $n=3$ ), with significant differences in mortality,  $p<0.001$ .

## ICU patients

Thirty-five patients (23.8%) required ICU admission. Twenty-three patients needed ventilator support with an average length of 7.5 days (SE 1.8). Inhalational injury was

reported in 4 patients (2.7%). The mean LOS at ICU was 18.7 days (SE 3.9). When compared by groups, the ICU admission data did not reveal statistical significance.

## Differences over the two periods (2008–2014 and 2015–2020)

A comparison of the two periods was made to reveal that the number of patients decreased from 106 to 41. The mean TBSA in 2008–2014 was 18.8% (SE 1.1), whereas during 2015–2020 such mean was 18.6% (SE 1.9), with no significant difference. Scalding was the most common cause of burns in both periods: 75 of 103 cases (70.8%) in 2008–2014, and 28 of 41 cases (68.3%) in 2015–2020. Among scald burns, hot water was the main mechanism (56 cases and 18 cases, 2008–2014 and 2015–2020, respectively). The number of operations required in 2008–2014 was 54 of 106 cases (50.9%), whereas the patients requiring surgery in 2015–2020 were 26 of 41 cases (63.4%). Mean length of stay for patients admitted for the first 6 years and for the later 6 years was 17.4 (SE 1.5) versus 28.8 (SE 7.2) days, respectively,  $p<0.05$ .

## Discussion

Although burn mortality appears to be decreasing over the years [5], pediatric burn injury still causes remarkable morbidity. The purpose of this study was to analyze the characteristics of children who suffer thermal injuries and to identify areas of potential intervention to reduce the incidence. The association of burn incidence with lower incomes areas is well documented [20]. However, data about family incomes were not collected for this study.

Our study revealed that the main mechanism of burn injury is scalding, followed by flame. This result is coincident with the described in the report of Mapfre Foundation and the Spanish Association of Burns (AEQUE) [9].

**Table 5** Complications according to %TBSA group

	TBSA $\leq 20\%$	TBSA $> 20\%$	Total
Wound infection	8	9*	17
Septicemia	0	8*	8
Ventilator-associated pneumonia (VAP)	3	9*	12
Nosocomial pneumonia	1	1	2
Urinary tract infection (UTI)	4	6*	10
Catheter-related bloodstream infections (CRBSI)	2	5*	7
Deep venous thrombosis (DVT)	0	1	1
Acute lung injury	0	2*	2
Toxic shock syndrome (Staphylococcus)	2	0	2
Total	18	41	59

\*  $p<0.05$



However, our mean TBSA was larger than the value reported in such study (18.7% vs 7.9%), likely because we excluded minor burn patients. Our data support that children under 6 years old represent more than 50% of admissions, and we noticed that younger children usually suffer scald burns while teenagers tend to suffer flame burns, probably caused by risk-taking activities with fire. In addition, more than a half of patients admitted were male. These data are similar to results shown in other studies [1, 5, 9, 21, 22].

The great majority of pediatric burns are accidental. However, a recent review of non-accidental burns in children [23] reported an incidence of 9.7%. In our series, only two cases (1.4%) of child abuse were detected, but this data might be underestimated. Physicians should suspect an intentional cause when children present additional injuries such as fractures, bizarre mechanisms of burn injury, or burns at certain locations as buttocks, genitalia, and legs. Non-accidental burns are associated with higher rates of length of stay and mortality [24].

While superficial partial thickness burns are usually treated with topical agents and dressings, some deep partial thickness and full thickness burns require escharectomy and skin grafting. These dressings require an appropriate sedation to reduce pain and anxiety, that are especially important factors in pediatric population under stress [25]. In the case of large TBSA burn patients, other options of coverage can be used such as cultured epithelial autografts (CEA), biological dressings (Biobrane®, Suprathel®, amniotic membrane...) or reconstructive flaps. In addition, some patients with deep burns may require escharotomies to avoid compartment syndrome.

Even though the use of bromelain (Nexobrid®) is currently off-label in pediatric population, some preliminary studies have shown its security, effectiveness, and selective non-surgical eschar removal in children, as well as a quicker debridement, lower incidence, and percentage area of surgical excision and grafting [26, 27]. These promising results will probably lead to a useful bromelain treatment in the future.

In our series, the group aged 13–18 showed significantly higher TBSA, more surgeries, and blood transfusions. Flame was the main mechanism in these patients. Although upper extremity was the most frequent location, group aged 13–18 also showed high rates of lower extremity injury.

Early fluid resuscitation is needed in patients with large TBSA burn to ensure an appropriate tissue perfusion. Furthermore, a significantly higher incidence of sepsis, renal failure, and mortality have been demonstrated when fluid resuscitation is initiated > 2 h after the burn [10]. Despite the importance of acute fluid resuscitation, there is no established consensus about the best formula to employ. Different fluid resuscitation formulas are used (Galveston, Parkland, BET...) [3, 28]. The Galveston resuscitation formula was the

most widely used, but the most appropriate formula for children is under controversy [3, 29]. Galveston formula consists of 5000 ml/m<sup>2</sup> body burn surface area plus 2000 ml/m<sup>2</sup> total body surface area. Lactated Ringer's solution with 12.5 g of 25% albumin per liter plus 5% dextrose is the fluid utilized in this formula. In contrast, Parkland formula provides 4 ml/kg/%TBSA burn of lactated Ringer's. In both cases half is given over the first 8 h and the remainder is given over the next 16 h. On the other hand, BET formula provides 220 ml/h/m<sup>2</sup> body burn surface area of human serum albumin with concentrations of 10, 7.5, 5, and 2.5% in lactated Ringer's (0–8, 8–16, 16–24, and 24–40 h post injury, respectively) [30]. Moreover, an early nutritional support has showed better outcomes in large TBSA patients [31].

Pediatric major burns are under severe metabolic stress and are immunocompromised leading to multiple complications including sepsis. The multiorgan failure caused by sepsis is actually the main reason of mortality in these patients [4]. An aggressive control of sepsis sources is mandatory to prevent complications. With greater TBSA values, more burn wound infection rates are detected in ICU patients [21]. Even in small area burns, children may develop a systemic inflammatory response without symptoms or initial signs of infection [32].

Higher rates of complications were detected in patients with TBSA values over 20%. The most frequent problems are related to infections, particularly important wound and respiratory infections. However, the evidence shows that systemic antibiotic prophylaxis is not effective to prevent infections in pediatric burn patients [33].

During the period of 12 years under study, the mortality rate of pediatric burn patients admitted to our hospital was low, at 0.7%, very similar to other studies [34]. The multidisciplinary approach (pediatricians, burn surgeons, physiotherapists, psychologists...) and many medical advances have contributed to improve mortality rates in major burn pediatric patients and this could be the reason of good outcomes in our study. As a whole, early burn excision, biological dressings, proper resuscitation and nutrition, control the sources of sepsis, limited blood transfusion, and rehabilitation are all factors that contribute to our low mortality rates. Size of burn and inhalation injury are correlated with the risk of mortality [5]. No differences were found in mortality among the 3 groups established in our study, limited by the low rates. Berndtson et al. [35] described a specific pediatric mortality score (Pediatric Risk of Mortality score) but it was not calculated because of missing data. Despite of fewer admissions in the second age period analyzed (2015–2020), the mean LOS was significantly higher. The lower rates of incidence in this second period could be due to a better understanding of parents about the burn risks and the positive effects of prevention campaigns on pediatric population carried out in the last years in Spain.

We should emphasize that scalds do not depend on a particular type of cooking, but rather on the parents' imprudence when they cook without watching appropriately their children. Specific prevention measures should be carried out to avoid burn injuries, as for instance, reducing the temperature of hot water to < 120 °F (48.9 °C), keeping children away from the kitchen, stoves, and fireplaces; turning pan handles to the back; disconnecting electronic devices; installing smoke detectors; and storing chemicals or flammable products.

Despite the retrospective observational nature of our study, we have focused on pediatric burn population because this specific topic is frequently excluded in major burns studies. However, some limitations should be taken into account. The purpose of our study was centered on major pediatric burns to analyze a more homogeneous group. If we had included minor burns, the results might be underestimated in terms of mortality and complications. In addition, certain patients with incomplete data would be excluded and the measure of TBSA would be imprecise to assess burn extension and severity. For these reasons, the initial estimation of TBSA was performed by 2 plastic surgeons and subsequently revised by an expert burn surgeon, which was present over the entire period of the study.

## Conclusions

In summary, scald burns are the most frequent mechanism of burn injury in pediatric major burns. However, teenagers usually suffer more severe burns and complications caused by flame and show a greater mean %TBSA. In all cases, more than 60% of patients were male. On the other hand, the number of admissions has been gradually reduced over the timeframe studied thus revealing the success of campaign preventions carried out on pediatric population in the last years in Spain.

Prevention campaigns are essential to reduce pediatric burns incidence and the multidisciplinary approach (especially with involvement of intensive care pediatricians) is the main key to achieve excellent results in terms of mortality and morbidity.

Altogether, early burn excision, proper resuscitation, control of the sources of sepsis, and management improvements are important factors that contribute to low mortality rates. The use of enzymatic debridement in pediatric population is absolutely encouraging, but more studies are needed.

**Abbreviations** AMR: Adjusted mortality rates; ICU: Intensive care unit; LOS: Length of stay; TBSA: Total body surface area; rBAUX: Revised Baux score; SE: Standard error

**Author contribution** JJ Pereyra-Rodriguez supervision, review draft and data curation. P. Gacto-Sanchez review draft. A. Garcia-Diaz written draft, data collection. All authors contributed to the study conception and design. All authors read and approved the final manuscript.

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## Declarations

**Ethics approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Approval was granted by the Ethics Committee of Andalusian Healthcare System (reference number 2680-N-20).

**Consent to participate** Informed consent was obtained from the parents and all individual participants included in the study.

**Conflict of interest** Antonio García-Díaz, Purificación Gacto-Sánchez, Antonio José Durán-Romero, Salvador Carrasco-García, Alejandro Ruiz-Moya, Julia Molina-Morales, María-Victoria Sánchez-Tatay, Tomás Gómez-Cía, and José-Juan Pereyra-Rodríguez declare no competing interests.

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