



## Education

# Incidence and risk factors for alopecia in survivors of critical illness: A multi-centre observational study



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## ABSTRACT

**Purpose:** To investigate the incidence, nature and risk factors for patient-reported alopecia in survivors of critical illness.

**Materials and methods:** A multi-centre, mixed methods observational study in the intensive care units (ICU) of ten hospitals in Wales. All patients with an ICU stay of 5 days or more, able to give consent were included. Demographic variables and risk factors were collected. A pre-designed survey was completed at three months post-ICU discharge. Statistical analysis included numbers and percentages (categorical variables) and medians and interquartile ranges (continuous variables). Comparisons between patients with and without alopecia were made using Fisher's Exact test (categorical variables) and Mann Whitney *U* test (continuous variables). Multivariate logistic regression analysis was used to determine the risk factors for alopecia.

**Results:** The survey was completed by 123 patients with alopecia reported in 44 (36%) patients. The only risk factor for alopecia on analysis was sepsis / septic shock ( $p < .001$ ; OR: 5.1, 95%CI: 2.1–12.4).

**Conclusions:** Limited research exists examining the incidence, nature and risk factors for patient-reported alopecia in adult survivors of critical illness. The results of this study highlight the need to discuss the potential for alopecia with survivors of critical illness, who had sepsis / septic shock.

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## 1. Introduction

Alopecia in adult survivors of critical illness has received limited attention in critical care research. During the acute critical illness phase, alopecia is of minimal concern to the intensive care team, when patient survival is the primary objective of medical management. In the recovery phase of illness however, alopecia can prove distressing for the patient [1,2]. It is further reported that many alopecia sufferers

experience feelings of distorted self-image, low self-esteem and may display symptoms of anxiety and depression [3]. Furthermore, medical treatment for the disorder has limited effectiveness, and the failure to find a cure can leave patients very distressed [3].

Alopecia has been reported to occur after severe psychological stress, multisystem illness and with drug administration [3–8] and various types of alopecia reported to occur in critically ill patients are telogen effluvium [4] pressure alopecia [5] and traction alopecia [9]. Incidence of pressure alopecia was summarised in a review by Davies and Yesudian (2012) who reported that alopecia is probably underreported in the literature and occurs following hypotensive or complicated surgery and prolonged stays in ICU, when patients require intubation [5]. The authors concluded that a prospective multi-centre study in high-risk cohorts (those undergoing prolonged surgery and patients intubated for long periods on ICU) may shed further light on this enigmatic condition.

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A single centre pilot study was completed prior to the commencement of this multi-centre study [10]. The pilot study recruited patients from its follow-up clinic and reported a 17% incidence of alopecia in their cohort. Similarly, a military cases series have described alopecia occurring in young, predominantly male populations recovering from severe trauma and reported a 35% incidence [11]. However, the incidence of alopecia for the wider critical care population is unknown. The aim of this study therefore was to investigate the incidence, nature and risk factors for patient-reported alopecia in a cohort of critical illness survivors.

## 2. Materials and methods

Ethical approval was given by the North of Scotland Research Ethics Service, 21/11/2016, Ref: 17/NS/0133. Written informed consent was given by all participants.

The study was completed in the ICU of ten hospitals in Wales between June 2017 and October 2017, with an additional three month follow up for survey completion. The participating units were a combination of both general medical and surgical specialties. The burns and paediatric units were excluded from the study. There are approximately 9300 admissions to the 15 Welsh critical care units each year [12]; the 10 participating units account for approximately 75% all critical care admissions in Wales [13]. Mean age of admissions to Welsh units (62 years) compared with UK case-mix programme mean 61 years) and APACHE II score (16 compared with UK case-mix programme average 15.3) is broadly similar to that of patients admitted to critical care units elsewhere in the UK (UK case-mix programme 2018); approximately 75% admissions are unplanned and 40% receive mechanical ventilation.

Patients were recruited to the study if they were aged 18 years or more, were considered to have capacity to give consent, were willing to complete a survey at three months post-ICU discharge and had an ICU length of stay of five or more days. This length of stay ensured a population was selected in whom more prolonged critical illness would be more likely to impact upon patient outcomes, as was used in previous critical care research [15]. Patients were excluded if they had pre-existing alopecia or baldness, or would be requiring chemotherapy following ICU discharge.

Eligible patients were approached for consent by the clinician leading the trial at each site, once the patient was awake and able to give consent (at least five days post-ICU admission). Demographic and risk factor data was collected prospectively for all study participants during their ICU stay either from the medical notes or using Ward Watcher (Critical Care Audit Ltd., West Yorkshire, England), a critical care database system used across Wales to collect data on patient demographics, presenting conditions, severity of illness, daily organ support, and outcome.

At three months post-ICU discharge, a pre-designed survey was sent to each participant, with a follow up phone call for completion, if the survey wasn't returned. One month was allowed for completion of the survey (either postal or telephone). The survey was developed using guidelines by Boyton et al. (2004) [16,17]. In order to assess the clinical sensibility of the survey, it was piloted on a number of ICU survivors attending our follow up clinic and as a result, a number of alterations were made to the survey design. Both closed and open-ended questions are used in the survey. (Survey available in supplementary material).

Data relating to baseline characteristics and critical care interventions were collected. The risk factors of particular interest a priori included: illness severity score (APACHE II score), ICU length of stay (whole days), number of organs requiring advanced support (either respiratory, cardiovascular or renal), need for blood transfusion and a diagnosis of sepsis / septic shock. The choice of risk factor was influenced by previous research [3–8] and our pilot study results. We adopted the method recently published by Shankar-Hari and colleagues (2017) to identify patients with sepsis and septic shock, according to the Third

International Consensus (Sepsis-3) Definitions [18,19]. An additional text file shows this method in more detail (see supplementary material).

Advanced respiratory organ support was defined as the number of days the patient required invasive mechanical ventilation, advanced cardiovascular support was defined as the number of days the patient received multiple inotropes/ vasopressors or an inotrope or vasopressor plus anti-arrhythmic treatment for one hour or more, and advanced renal support was defined as the number of days the patient received haemofiltration and/or haemodialysis.

The original sample size proposed for this study was 400 patients, based on our previous pilot work which reported a 17% incidence of alopecia [10]. Vittinghoff and McCulloch (2007) suggested that the number of patients needed to ensure sufficient power in a cohort study is equivalent to five to nine events per variable (EPV) being investigated [20]. We aimed to investigate five variables or risk factors (using an EPV of 8), therefore a minimum of 40 events (incidence of alopecia) were required.

Statistical analysis was completed using SPSS (version 22) and included numbers and percentages (categorical variables) and medians and interquartile ranges (continuous variables). Comparisons between patients with and without alopecia were made using Fisher's Exact test (categorical variables) and Mann Whitney *U* test (continuous variables). Non-responder analysis was also completed, to test for differences between participants not returning the surveys. For the multivariate analysis, logistic regression with backward stepwise elimination by using the likelihood test statistic was used to assess potential risk factors for alopecia in survivors of critical illness. All prognostic variables were included in the final analysis [21]. Adjusted odds ratios and the 95% confidence intervals were calculated for each risk factor. Missing data was handled using a simple imputation of the mean, as <10% of data was missing. Statistical significance was set at  $p < .05$ .

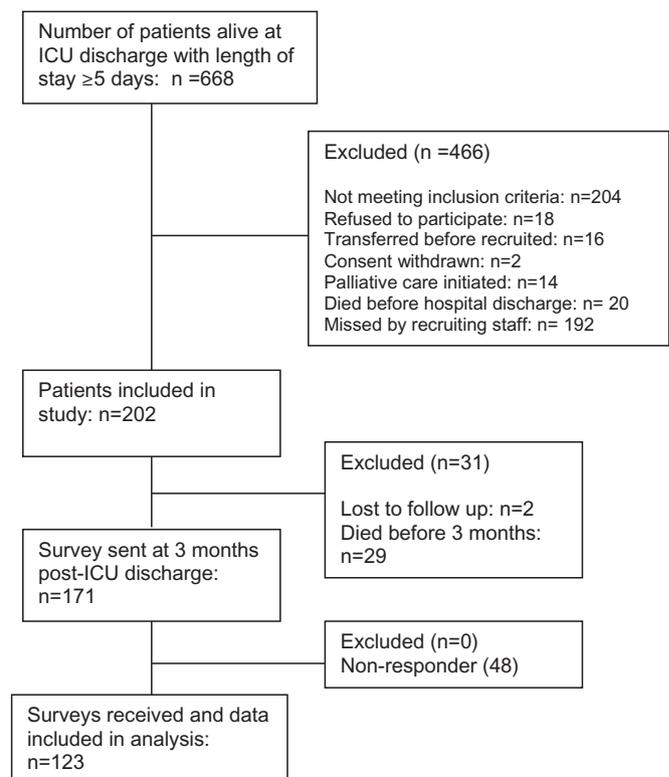


Fig. 1. Flow of patients through study.

### 3. Results

Fig. 1 demonstrated the flow of patients through the study. There were 44 (36%) reported cases of alopecia in the cohort of ICU survivors.

Table 1 highlights the baseline patient characteristics and critical care interventions respectively for the 123 patients included in the final analysis.

Analysis was completed to investigate any difference between the responders and non-responders. The non-responders were found to be significantly younger than the responders ( $p = .027$ ) and there was a significantly higher number of males who returned the survey ( $p = .041$ ). There were no differences in any other variables investigated.

Table 2 demonstrates the results of the survey, for the participants reporting alopecia. A sudden on-set of alopecia was reported in 11 (25%) patients, compared to 24 (55%) patients, who stated it started gradually (with nine unsure). No patients reported associated pain or swelling with the alopecia and 39 (89%) patients stated the alopecia was confined to the scalp. No patients had sought medical assistance for the alopecia, with eight (18%) patients reporting that they used a new shampoo or oil to try to address the problem.

The results of the univariate analysis are outlined in Table 3. The only risk factor for alopecia in survivors of critical illness was a diagnosis sepsis/septic shock ( $p < .001$ ; odds ratio: 8.5; confidence interval: 3.4–21.2).

The results of the multivariate logistic regression analysis are shown in Table 4. The only risk factor for alopecia in survivors of critical illness was a diagnosis of sepsis / septic shock ( $p < .001$ ; odds ratio: 5.1; confidence intervals: 2.1–12.4).

### 4. Discussion

Alopecia has been reported for many years in ICU survivors, but to date, no study has been completed reporting its incidence, nature or risk factors. In this study, 36% of patients reported suffering from alopecia at three months post-ICU discharge. Sepsis was the only significant risk factor on logistic regression analysis for alopecia in survivors of critical illness in this study. It seems likely that this reflects the reduction in tissue perfusion which occurs in sepsis but interestingly serum lactate did not differ significantly between the two groups, nor did the APACHE II illness severity score predict the development of alopecia. Clearly further research is required to investigate the pathophysiological processes occurring in critical illness and sepsis which predispose to alopecia. In addition, improved knowledge of certain risk factors may facilitate research into dermatological conditions or new bedside interventions to minimise the condition. Furthermore, research into the consequences of alopecia for the individual, or particular patient groups within the ICU cohort is needed.

The incidence of alopecia in this study was twice the reported incidence that we reported in our pilot work [10]. This multi-centre study builds on the work of the pilot study, as risk factors were not considered in the pilot work and patients were only recruited from the follow-up clinic, leading to potential selection and recall bias.

A previous study investigating outcomes in a cohort of military intensive care survivors reported occipital alopecia in 35% of patients [11]. However, for this military population, occipital alopecia appeared to occur in conjunction with the development of occipital pressure ulceration, a phenomenon not reported by participants in our study among whom trauma was an infrequent cause of critical illness [11]. The most common type of hair-loss reported in our study was all over

**Table 1**  
Baseline patient characteristics and critical care interventions during ICU stay.

Characteristic	All patients (n = 123)	No alopecia (n = 79)	Alopecia (n = 44)	p value
Age (years)	67 (55–75)	67 (58–76)	67 (48–71)	$p = .159$
Sex (male)	69 (56%)	49 (62%)	20 (45%)	$p = .127$
APACHE II score	16 (11–20)	16 (12–20)	16 (11–22)	$p = .776$
ICU length of stay (days)	8 (6–13)	8 (6–11)	9 (6–17)	$p = .152$
Primary admission diagnosis				$p = .394$
Medical	57 (46%)	39 (50%)	18 (41%)	
Surgical	53 (43%)	30 (38%)	23 (52%)	
Trauma	9 (7%)	7 (8%)	2 (5%)	
Neurological	4 (3%)	3 (4%)	1 (2%)	
Emergency surgery	39 (32%)	21 (27%)	18 (41%)	$p = .111$
Pre-existing conditions:				
Chronic Kidney disease	6 (5%)	3 (4%)	3 (7%)	$p = .664$
Malignant disease in last 3 years	24 (20%)	18 (23%)	6 (14%)	$p = .341$
Anaemia	4 (3%)	2 (3%)	2 (5%)	$p = .613$
Auto-immune disease	10 (8%)	7 (9%)	3 (7%)	$p = 1.000$
Sepsis/septic shock diagnosis	32 (26%)	9 (11%)	23 (52%)	$p < .001$
Serum lactate	1.8 (1.2–3.3)	1.8 (1.2–2.9)	1.9 (1.2–3.0)	$P = .555$
Weight loss during ICU stay (kg)	1 (0–2.5)	1 (0–2)	0.5 (0–3.8)	$p = 1.000$
Advanced cardiovascular support (days)	0 (0–0)	0 (0–0)	0 (0–0)	$p = .582$
Advanced respiratory support (days)	2 (0–6)	2 (0–5)	2 (0–6)	$p = .279$
Advanced renal support (days)	0 (0–0)	0 (0–0)	0 (0–0)	$p = .617$
CPR in 24 h prior to admission	5 (4%)	2 (3%)	3 (7%)	$p = .344$
Blood transfusions received	22 (18%)	15 (19%)	7 (16%)	$p = .808$
ICU medications received				
Thyroxine	12 (10%)	8 (10%)	4 (4%)	$p = 1.000$
Steroids	21 (17%)	15 (19%)	6 (14%)	$p = .618$
ACE-inhibitors	32 (26%)	18 (23%)	14 (32%)	$p = .291$
Anti-hypertensives	55 (45%)	39 (49%)	16 (36%)	$p = .187$
Anti-depressants	24 (20%)	16 (20%)	8 (19%)	$p = 1.000$
Anti-convulsants	4 (3%)	2 (3%)	2 (5%)	$p = .613$
Anti-hyperlipidaemics	36 (29%)	24 (30%)	12 (28%)	$p = .838$

CPR: cardiopulmonary resuscitation.

Results in medians (IQR) or numbers (%). Comparisons between patients with and without alopecia were made using Fisher's Exact test (categorical variables) and Mann Whitney U test (continuous variables).

**Table 2**  
Results of survey; nature of alopecia.

Time from ICU discharge to on-set of hair-loss	During ICU admission	1–2 weeks	3–4 weeks	5–6 weeks	7–8 weeks	9–10 weeks	11–12 weeks	≥13 weeks	Unsure
Number (%) of patients	1 (2%)	14 (32%)	17 (39%)	2 (5%)	6 (14%)	0 (0%)	1 (2%)	1 (2%)	2 (5%)
Type of onset	Suddenly	Gradually	Not sure						
Number (%) of patients	11 (25%)	24 (55%)	9 (20%)						
Type of hair-loss	Coin shaped bald spots normal scalp	Localised hair loss abnormal scalp	One or more areas of thinning	All over thinning	More than one type				
Number (%) of patients	3 (7%)	1 (2%)	7 (16%)	28 (64%)	5 (11%)				
Associated pain or swelling	Yes	No	Not sure						
Number (%) of patients	0 (0%)	44 (100%)	0 (0%)						
Alopecia confined to scalp	Yes	No	Not sure						
Number (%) of patients	39 (89%)	5 (11%)	0 (0%)						
Location of hair-loss	All over	Front	Back	Top	Sides	More than one			
Number (%) of patients	17 (39%)	1 (2%)	3 (7%)	11 (25%)	2 (5%)	10 (23%)			
Severity of hair-loss	Minor (<10%)	More than minor (<25%)	Major (<50%)	Severe (>50%)	Unsure				
Number (%) of patients	20 (45%)	16 (36%)	4 (9%)	2 (5%)	2 (5%)				
Time hair-loss lasted	On-going	1–2 weeks	3–4 weeks	5–6 weeks	7–8 weeks	9–10 weeks	11–12 weeks	≥13 weeks	Unsure
Number (%) of patients	10 (23%)	3 (7%)	12 (27%)	0 (0%)	7 (16%)	0 (0%)	8 (18%)	1 (2%)	3 (7%)
Time until regrowth from discharge	No regrowth	1–2 weeks	3–4 weeks	5–6 weeks	7–8 weeks	9–10 weeks	11–12 weeks	≥13 weeks	Unsure
Number (%) of patients	29 (66%)	1 (2%)	4 (9%)	1 (2%)	0 (0%)	1 (2%)	4 (9%)	3 (7%)	1 (2%)
Alopecia treatment received	Yes	No	Not sure						
Number (%) of patients	0 (0%)	44 (100%)	0 (0%)						
Intervention to restore hair	Yes	No	Not sure						
Number (%) of patients	8 (18%)	36 (82%)	0 (0%)						

Data presented as numbers (percentages).

thinning, ranging from minor to severe, starting within the first month following ICU discharge and still on-going, with no signs of regrowth at the time of survey completion. The difference in the results may be due to inherent differences in the study populations, as the military population had a higher proportion of males, were younger and had a longer median length of stay in ICU than this study.

The clinical implications of this study primarily relate to the distressing nature of alopecia for the patients in their recovery process. Alopecia in this population has been recognised and acknowledged as distressing for patients in critical care literature for at least 20 years [1,2]. Critical illness survivors commonly report how upsetting it is to suffer alopecia and there are many examples on the ICUsteps website (UK-based ICU support charity run by former ICU patients and relatives) on-line patient forum which emphasises the impact of this condition on patients' lives [22]. This is the first multi-centre study that has attempted to address the problem. The next phase of this work is to examine the impact of alopecia on this patient cohort through the completion of a qualitative study.

It is not possible at this stage to make recommendations for change in clinical practice, based on this study's findings. Further research is now needed to identify the pathophysiological processes of sepsis / septic shock that seem to be causing alopecia in this patient population.

However, an understanding that this is a relatively common phenomenon arising from critical illness may to some extent help individuals come to terms with the condition.

There are a number of limitations in this study. Not achieving our target sample size may have influenced the results and affected the power of the study however, sufficient number of cases of alopecia allowed the original planned analysis. Although a 72% response rate was achieved with the surveys, reporting bias may have also influenced the results as patients without alopecia may have been less inclined to return the survey. Non-responder analysis demonstrated the patients not returning the survey were significantly younger and more were female.

A formal examination by a doctor was not completed as part of study, which would have supported the patients' own findings and could have provided information regarding potential aetiology of the alopecia. This would also limit the ability of the study to identify a pre-existing alopecia condition that worsens during the ICU stay, compared to a new on-set alopecia of a specific aetiology. Not including patients who lacked capacity to complete the survey may have resulted in exclusion of sicker patients, thus influencing the study results. Hormonal differences in males, pre and post-menopausal females may also have influenced the study results.

**Table 3**  
Results of univariate analysis.

Risk factor	All patients (n = 123)	No alopecia (n = 79)	Alopecia (n = 44)	p value; unadjusted odds ratio (95% CI)
APACHE II score	16 (11–20)	16 (12–20)	16 (11–22)	p = .776; 3.8 (0.4–177.9)
ICU length of stay	8 (6–13)	8 (6–11)	9 (6–17)	p = .152; 1.5 (0.6–3.9)
Sepsis/septic shock	32 (26%)	9 (11%)	23 (52%)	p < .001; 8.5 (3.4–21.2)
Blood transfusion	22 (18%)	15 (19%)	7 (16%)	p = .808; 0.8 (0.3–2.2)
Number of organs supported	1.0 (0.0–1.0)	1.0 (0.0–1.0)	1 (0.3–1.8)	p = .244; 1.3 (0.8–2.2)

n: number, CI: confidence interval.

Comparisons between patients with and without alopecia were made using Fisher's Exact test (categorical variables) and Mann Whitney U test (continuous variables).

**Table 4**  
Results of multivariate logistic regression analysis.

Risk factor	p-Value	Adjusted odds ratio	95% CI
APACHE II score	0.900	1.0	0.9–1.1
ICU length of stay	0.854	1.0	0.9–1.0
Sepsis/septic shock	<0.001	5.1	2.1–12.4
Blood transfusion	0.514	0.7	0.2–2.1
Number of organs supported	0.812	0.9	0.5–1.6

CI: Confidence interval. Analysis completed using logistic regression with backward stepwise elimination by using the likelihood test statistic.

## 5. Conclusions

In conclusion, this study has demonstrated that alopecia is a common problem in survivors of critical illness. Due to the distressing nature of the condition, the potential for alopecia to occur in the recovery phase of critical illness should be communicated more widely with patients and their relatives, especially when sepsis has been identified. Further research is needed into the pathophysiological mechanisms causing alopecia, in order that potential preventative measures can be taken during the ICU stay.

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## Conflict of interest statement

There are no conflicts of interest to declare.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcrc.2018.11.015>.

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