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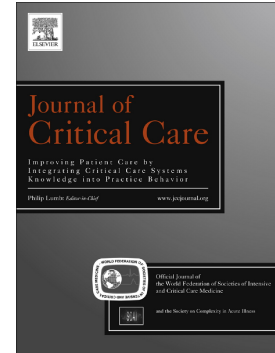
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Health-Related Quality of Life After Obstetric Intensive Care Admission: Comparison with the General Population

CONFLICT OF INTEREST

The authors have disclosed that they do not have any potential conflict of interest.

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ABSTRACT

Purpose: To examine health-related quality of life (HRQoL) in obstetric patients after intensive care discharge, with comparison to age-appropriate reference values from the general Finnish female population.

Material and methods: Retrospective register-based study. Four multidisciplinary intensive care units at Finnish university hospitals participated.

Results: A total of 291 obstetric patient were admitted to the ICU, of whom 114 (39 %) completed follow-up measurements. At baseline (pre-intensive care admission), patients showed lower physical (mobility, self-care, pain/discomfort) and social (usual activities) dimensions compared to reference values. Baseline overall health status (EQsum) was lower than reference values. However EQsum increased over six months (mean, 0.907 to 0.946) such that follow-up values were similar to reference values. At follow-up, 18.4% of patients showed poorer HRQoL (mean, 0.764; range, 0.638–0.885) compared to reference values. Multiparous patients showed lower scores than primiparous patients. EQ VAS scores were lower at baseline, but increased over six months (72.12 to 87.5) such that follow-up values were similar to reference values.

Conclusions: The baseline HRQoL of study population was lower than that of the general population, but after six months, the mean values were comparable to reference value. However, one in five patients still experienced impaired QOL at follow-up.

Key Words: critical care; obstetric labor complications; pregnancy complications; quality of life

INTRODUCTION

In developed countries, maternal mortality has decreased to very low rates [1]. However, pregnancy and childbirth are still potentially associated with severe maternal morbidity, sometimes requiring maternal intensive care. Leading causes of pregnancy-related admissions to the intensive care unit (ICU) are hypertensive complications and obstetric hemorrhage [2-8]. In addition, non-obstetrical indications, such as exacerbation of chronic disease, can necessitate ICU admission [9].

Even in cases of critical illness, obstetric patients commonly show good short-term outcomes in developed countries [10]. However, pregnancy and delivery are still potentially life-threatening situations. Moreover, when women require obstetric postpartum intensive care, the newborn may also be in bad condition and receiving intensive care [9, 11]. Such pregnancy- and delivery-related complications can influence an obstetric patient's physical, mental, and social well-being, exacerbating reductions of health-related quality of life (HRQoL) over a longer period [12]. Despite increasingly awareness of the long-term effects of critical illness in the general population, obstetric patients are an often neglected group in research.

The aim of our present study was to examine HRQoL in obstetric patients after intensive care discharge, with comparison of our results to age-appropriate reference values from the general Finnish female population. Our hypothesis was that at six months following ICU discharge, the patients' health status would have returned to normal with no remaining physical, social, or mental problems. HRQoL was measured using the EuroQol-5D (EQ-5D) tool, including a summary index (EQsum) and visual analogue scale (EQ VAS).

MATERIALS AND METHODS

Study Design and Population

This retrospective register-based study included data on obstetric patients treated in the intensive care units of four Finnish university hospitals, during pregnancy and up to 42 days post-partum, over a five-year study period. The study protocol received ethics committee approval (R12050H), and the National Institute for Health and Welfare (THL) granted permission for data collection and to maintain the study register. Data were collected from the Medical Birth Register (MBR), which is maintained by THL and includes maternal sociodemographic and obstetric information for all mothers who have given birth in Finland, as well as perinatal outcomes for up to seven days for all live-born or stillborn infants born after 22 weeks of gestation or weighing \geq 500 g. Data were also retrieved from the following clinical information systems (CIS): Clinisoft, the Finnish Intensive Care Quality Consortium (Intensium, Kuopio, Finland), and the Miranda database.

Data Collection

From the Intensium hospital database, we identified obstetric patients of 18–50 years of age, who were treated in the ICU during pregnancy and postpartum, with discharge dates from January 1, 2007 to December 31, 2011. Searches were performed using the APACHE III classification “other gynecological disease”. Exclusion criteria were not being an obstetric patient, maternal death in the ICU, missing MBR data, or missing EQ-5D measurement (baseline and follow-up).

Data from the hospital database were linked with the MBR using the patients' personal identification numbers. The database included the following information on maternal and neonatal characteristics: age; previous deliveries; number of fetuses; gestational age, i.e., normal, late preterm, moderately preterm, or extreme preterm; delivery type, i.e., vaginal,

planned caesarean section (CS), urgent CS, or emergency CS; admission cause, including obstetric reasons (e.g., hypertensive complications, obstetric hemorrhage, or other pregnancy- or delivery-related complications) and non-obstetric reasons (e.g., heart disease, respiratory failure, infection, liver or kidney dysfunction, or miscellaneous); ICU interventions, such as mechanical ventilation, CPAP/BiPap, hemodialysis, , arterial pressure, central line, and pulmonary artery catheter; ICU scores, i.e., APACHE II, SAPS II, SOFA, and TISS-76 daily and total; length of stay; treatment administered to newborn children, i.e., intensive care or observation unit; and perinatal mortality.

Health-Related Quality of Life Measurement

Health-related quality of life (HRQoL) was measured using the generic EuroQol 5D (EQ-5D) instrument. The EQ-5D includes two parts, the first of which measures health in five dimensions: the physical dimensions of mobility, self-care, and pain or discomfort; the mental dimension of depression or anxiety; and the social dimension of usual activities (work, study, homework, family, or leisure activities). Respondents asked to choose the most suitable option from three alternatives—no problem (1), moderate problems (2), of severe problems (3)—making it possible to define various health states as a digital number series. These preference-based measures are used to calculate a single summary index score (EQsum) based on the different aspects of health, which ranges from 0 to 1.0. The second part of the EQ-5D is a self-rated visual analogue scale (EQ VAS), used to rank health from 0 (worst imaginable health state) to 100 (best imaginable health state) [13].

EQ-5D measurement was a standard part of case management in the intensive care process in the units from which data was collected for our present study. For the baseline measurement, an intensive care nurse or physician asked the patient the EQ-5D questions referred to the time preceding the acute hospitalization. The collected data were recorded in the

CIS (Clinisoft). Since the data were routinely collected and retrospectively analyzed data, the data collection was consistent throughout the study period. Follow-up measurements were collected via telephone interview or letter at six months after ICU discharge. Follow-up data were collected and recorded by nominated persons in each unit. The obstetric patients' HRQoL measurements included information from the of EQ-5D dimensions and EQ VAS. The EQsum was calculated by one of the authors [15].

Statistical Analysis

Data analyses were performed using SPSS 15.0 software (SPSS, Chicago, IL). Categorical data are presented as percentages. Continuous data showed a non-normal distribution and are reported as median and interquartile range (IQR 25th–75th percentiles). EQ-5D population norms are reported in the literature [14], including defined reference values for the general Finnish population, including for both genders and multiple age groups [15]. Reference values were obtained from the general Finnish population of females aged 17–44 years. Finnish population mean reference scores (EQsum) were relatively stable from 17 to 44 years (from 0,96 to 9,93), as well as EQ-VAS (around 86) [15]. Impaired QOL at follow-up was defined as measurements lower than the reference population values minus the clinically important difference, which was 0.074 for EQsum [16]. Comparisons were performed using the Mann-Whitney U test and Fisher's exact test. A p value of <0.05 was considered significant in all tests.

RESULTS

Characteristics

During the study period, 328 admissions were recorded as "other gynecological disease" according to the APACHE III classification. Of these admissions, 99 were excluded: 54

were missing EQ-5D measurement (baseline and follow-up), 37 were non-obstetric patients, 7 were missing BR data, and 1 admission resulted in maternal death. Thus, a total of 229 obstetric patients were eligible for analysis, with available data from CIS, MBR, and EQ-5D measurements (baseline and/or follow-up). We analyzed a total of 214 baseline EQ-5D measurements (from before the ICU stay) and 114 follow-up EQ-5D measurements (from six months after pregnancy and ICU discharge). A total of 115 patients were lost to follow-up (**Fig. 1**). Table 1 presents the follow-up characteristics of the patients with normal QOL ($n = 93$), patients with impaired QOL ($n = 21$), and those lost to follow-up ($n = 115$).

EQ-5D Dimensions

Compared to reference values, the patients showed impaired baseline EQ-5D results in the physical dimensions (mobility, self-care, pain or discomfort) and the social dimension (usual activities) (**Fig. 2**). These values were increased at six months after ICU discharge, such that the follow-up values did not significantly differ from the reference values. The EQ-5D results for mental quality of life at baseline and follow-up in patients did not differ from the reference values.

EQsum and EQ VAS

The baseline mean EQsum score was 0.907, which was lower than reference values (**Table 2**). Moreover, the reference values were also higher than the baseline EQsum scores in the age groups 18–24 years and 25–34 years. For 93 patients (81.6%), health status had returned to normal at six months after ICU discharge (mean EQsum, 0.987; range, 0.885–1) relative to the reference values. On the other hand, 21 patients (18.4%) reported decreased HRQoL at follow-up (mean, 0.764; range, 0.638–0.885) compared to the reference values (**Table 3**). Of these patients, 14 (66%) had decreased HRQoL compared to baseline (0.982 to 0.766), five (24%) had HRQoL

similar to baseline (0.742 to 0.746), one (5%) had HRQoL increased from baseline (0.559 to 0.745), and one (5%) had a missing baseline measurement. Multiparous women scored worse on their HRQoL compared to primiparous women. At the baseline 132 patients had ICU LOS <24 hours and 82 had LOS \geq 24 hours. Statistically, ICU LOS and HRQoL at baseline did not differ between the groups ($p = 0.472$). The baseline mean EQ VAS score was 72.12, which was lower than the reference value. Six months after discharge, self-rated health status had returned to normal compared to the reference values (**Table 3**).

DISCUSSION

In our present study, we examined HRQoL in obstetric patients treated in intensive care units and compared the results to age-appropriate reference values from the general Finnish female population. During the study period there were 94 642 births in four hospital districts and 291 obstetric ICU admissions (0.3% of all maternities; varied 0.02 to 0.5 %). Our findings demonstrated that obstetric patient health status was lower than reference values prior to ICU admission, and had returned to reference value levels by six months following ICU discharge. However, nearly one-fifth of patients still had below-reference value HRQoL at follow-up.

In the current study, we found that physical QOL values at the end of pregnancy were lower than reference values. Prior studies show that pregnant women experience poor physical and mental HRQoL. Tsai et al (2016) reported impaired physical and mental HRQoL that persisted throughout the entire pregnancy. Compared to controls, Sut et al (2016) found pregnant women had worse EQ-5D scores, with decreases in the second and third trimesters. In particular, scores on the physical dimension reportedly decrease from early to late pregnancy [19, 20]. Prior studies report that sleep disturbances are a contributing factor to the poor QOL experienced by pregnant women [17, 18], and that delivery by elective or emergency CS negatively impacts

physical [21] and perceived HRQoL [22]. Interestingly, our present results showed that scores on the depression or anxiety dimension among patients were similar to reference values, indicating that pregnancy or delivery did not affect mental HRQoL.

Our present findings partly support the hypothesis that health status returned to reference values by six months after ICU discharge. However, nearly one-fifth of the study patients still had lower HRQoL at 6 months after discharge. In this study given the low severity of illness and the very short length of ICU stay, it seems unlikely that the ICU admission itself would have any major long-term impact on HRQoL. Van der Voude et al. (2015) found in their review that incontinence and being HIV-positive seemed to be associated with impaired QoL in postpartum women. In addition, postpartum depression and a caesarean section seemed to be associated with impaired health status.

In their study of women admitted to the ICU for non-obstetric reasons, Cartin-Ceba et al (2008) found that maternal critical illness and specific ICU interventions significantly affected fetal outcomes. Although our present study included a low number of non-obstetric admissions, over half of the neonates in such cases were preterm and required treatment in the NICU or observation unit. Notably, the emergency section rate was also higher in this group, although this difference was not statistically significant. Previous studies of general obstetric population care have reported mothers of very low birthweight infants experienced worse physical and mental HRQoL than mothers of normal birthweight infants [24]. Although our present results showed no significant association between long-term HRQoL and these neonate outcomes, others have reported that NICU admission and perinatal death are associated with decreased long-term QoL [25].

When evaluating the present study results and the data available in the literature, it is important to realize that impaired HRQoL after follow-up is not necessarily caused by the

intensive care treatment. These present results demonstrate considerably better HRQoL than found in the general ICU population [26]. It is likely that HRQoL is largely predicted by a combination of obstetric complications, such as hypertensive disorders, obstetric hemorrhage, delivery-related complications, and neonatal outcomes, rather than critical care admission alone. The therapeutic needs of obstetric patients differ from the needs of other populations admitted to the ICU. The duration of ICU stay in our present series was lower than reported by others [2, 4, 8], as was the need for assisted ventilation [7, 8]. However, similar to previously reported findings, hypertensive disorders and hemorrhage were the leading causes of obstetric ICU admissions in our present population [10]. Saravanakumar et al (2008) reported a large sample of patients who received high dependency unit care in obstetric settings, and reported that hypertensive disorders and obstetric hemorrhage were the most frequent reasons for admission. Furthermore, length of stay was typically less than a day, and the need for intervention was minor.

After intensive care discharge HRQoL improves over time, with obstetric ICU patients showing good long-term outcomes. However, in our present study population of obstetric patients, at six months after discharge, 21.9% still experienced pain or discomfort and 11.4% still experienced depression or anxiety. It is essential to identify the patients who are more likely to require physical or mental support after intensive care discharge. Our results indicated that impaired QOL at follow-up was particularly common among multiparous patients. However, this may be related to factors associated with being multiparous, and has nothing at all to do with the ICU admission. In further studies multidimensional measurements to describe ICU admitted obstetric patient physical, cognitive and psychological components in long-term period should be considered.

Our present study has several limitations. First, the addition of more time-points beyond six months after discharge could have provided additional information about long-term

HRQoL in this population. However, a six-month follow-up is considered adequate [28]. Second, it would have been more informative to make comparisons with a pregnant non-ICU patient population and a maternity ward population. Alternatively, it can be hypothesized that complete recovery from intensive care is more likely in an obstetric population than a non-pregnant population. Finally, although our sample size was reasonable compared to previous studies [26], a considerable number of patients were lost to follow-up. A risk of bias is caused by the majority of patients being lost to follow-up. Strengths of this study include the multicenter design, and the observation of all obstetric ICU admissions during the five-year study period with standard assessment of HRQoL at baseline.

CONCLUSIONS

Obstetric patient health status at baseline was lower than that of the reference population, but was similar to reference values at six months after pregnancy and intensive care discharge. However, one in five patients still experienced impaired QOL at follow-up.

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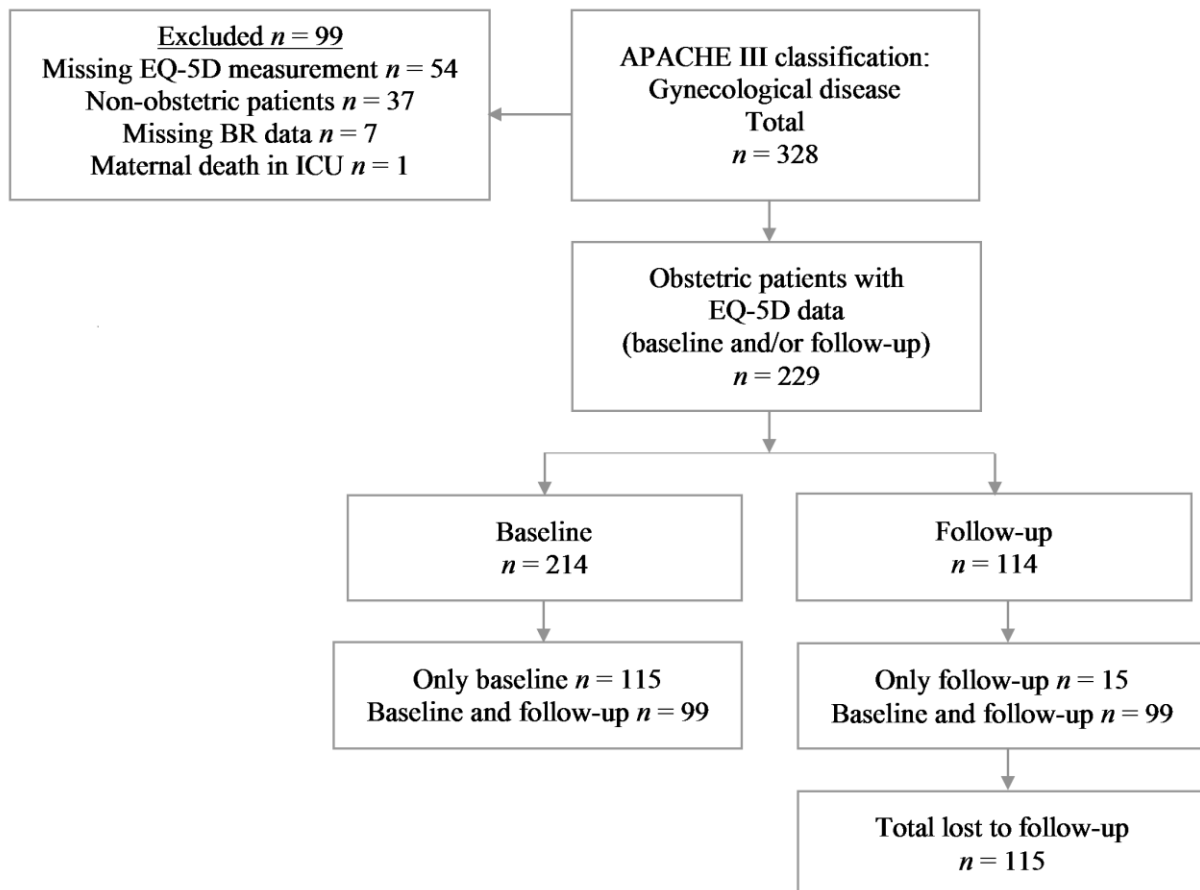


Fig. 1

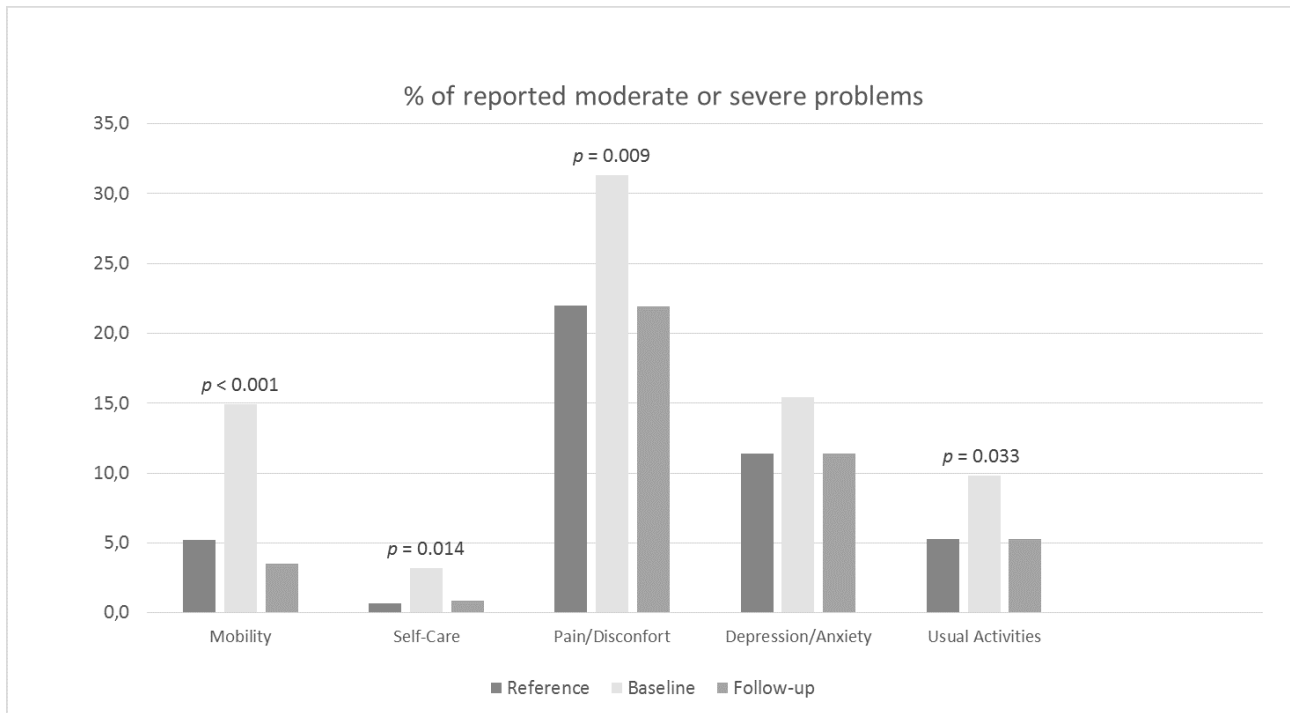


Fig. 2

TABLE 1. Follow-up Characteristics of Intensive Care Unit Admitted Obstetric Patients

Maternal characteristics	Normal QOL ^a (<i>n</i> = 93) <i>n</i> (%)	Impaired QOL (<i>n</i> = 21) <i>n</i> (%)	Lost to follow up (<i>n</i> = 115) <i>n</i> (%)	<i>p</i>
Age in years, median (IQR)	30.0 (27.0-34.0)	32.0 (30.5-38.0)	31.7 (27.1–36.0)	0.139
Previous deliveries				
0	62 (66.7)	9 (42.9)	68 (59.1)	0.003
1–2	29 (31.2)	7 (33.3)	37 (32.2)	
≥3	2 (2.2)	5 (23.8)	10 (8.7)	
Gestational age ^b				
Normal	45 (48.4)	7 (35.0)	50 (43.5)	0.299
Late preterm	25 (26.9)	4 (20.0)	22 (19.1)	
Moderately preterm	20 (21.5)	8 (40.0)	30 (26.1)	
Extremely preterm	3 (3.2)	1 (5.0)	13 (11.3)	
Delivery type				
Vaginal	22 (23.7)	3 (14.3)	20 (17.4)	0.081
Planned section	11 (11.8)	2 (9.5)	13 (11.3)	
Urgent section	57 (61.3)	12 (57.1)	68 (59.1)	
Emergency section	3 (3.2)	4 (19.0)	14 (12.2)	
Admission cause				
Hypertensive complications ^c	57 (61.3)	12 (57.1)	61 (53.0)	0.947
Hemorrhage	21 (22.6)	5 (23.8)	22 (19.1)	
Pregnancy or delivery related	10 (10.8)	3 (14.3)	21 (18.3)	
Non-obstetric complications	5 (5.4)	1 (4.8)	11 (9.6)	
Interventions				
Mechanical ventilation	19 (20.4)	4 (19.0)	23 (20.0)	1.000
CPAP/BiPap	6 (6.5)	-	5 (4.3)	0.591
Hemodialysis	-	-	2 (1.7)	-
Arterial pressure catheter	91 (97.8)	20 (95.2)	112 (97.4)	0.460
Central line	30 (32.3)	5 (23.8)	29 (25.2)	0.602
Pulmonary artery catheter	2 (2.2)	2 (9.5)	3 (2.6)	0.154
ICU scores, median (IQR)				
APACHE II	9.0 (7.0–12.0)	10.0 (6.5–12.5)	9.5 (7.0–12.0)	0.560
SAPS II	15.0 (10.0–21.0)	14.0 (10.0–19.0)	14.0 (10.0–21.0)	0.856
SOFA	3.0 (2.0–5.0)	2.0 (1.0–5.5)	2.0 (1.0–4.0)	0.934
TISS-76, daily	20.5 (18.5-24.5)	24.5 (18.8-27.9)	21.5 (17.5-26.0)	0.129

TISS-76, total	41.0 (35.5–50.5)	44.0 (32.0–72.5)	41.0 (32.0–53.0)	0.456
Length of ICU stay (hours), median (IQR)	21.0 (16.0-27.0)	20.0 (12.5-33.0)	21.0 (15.0-28.0)	0.709
Number of newborns	<i>n</i> = 104 (%)	<i>n</i> = 22 (%)	<i>n</i> = 123 (%)	
Treatment to newborn in NICU or observation unit	54 (51.9)	15 (68.2)	64 (52.0)	0.238
Perinatal mortality ^d	3 (2.9)	2 (9.1)	5 (4.1)	0.209

^a Compared to age-appropriate reference values from the Finnish female population.

^b Gestational age in weeks: normal, ≥ 37 ; late preterm, 34^{+0} – 36^{+6} ; moderately preterm, 28^{+0} – 33^{+6} ; extremely preterm, < 28 .

^c Pre-eclampsia, eclampsia and hypertension.

^d Stillborn or died before seven days of age.

TABLE 2. Summary Index (EQsum) and Visual Analogue Scale (EQ-VAS) Scores from Patients Compared with the General Finnish Female Population (GP) by Age Groups

EuroQol-5D measurement	Age, years										All	
	18-24			25-34			35-44					
		n	p	n	p	n	p	n	p	n	p	
EQsum												
GP	0.96	166		0.95	213		0.93	170		0.946	549	
baseline	0.894	28	<0.05	0.912	126	<0.01	0.903	60	ns	0.907	214	<0.001
follow-up	0.940	13	ns	0.954	73	ns	0.926	28	ns	0.946	114	ns
EQ-VAS												
GP	87	166		87	213		85	170		86.38	549	
baseline	72.19	21	<0.05	68.71	77	<0.001	75.48	33	<0.05	72.12	131	<0.001
follow-up	89.16	12	ns	87.16	61	ns	87.52	25	ns	87.5	98	ns

Ns = nonsignificant.

TABLE 3. Summary Index (EQsum) at Baseline and Follow-up in Patients with Impaired Health Related Quality of Life

EQsum	<i>n</i>	Baseline		Follow-up	
		Mean	Min–max	Mean	Min–max
All	21	0.901	0.559–1	0.764	0.638–0.885
Increased	1	0.559		0.745	
Similar	5	0.742	0.62–0.885	0.746	0.693–0.824
Decreased	14	0.982	0.833–1	0.766	0.638–0.885
Missing baseline	1			0.833	

Highlights

- After intensive care discharge HRQoL improves over time, with obstetric ICU patients showing good long-term outcomes
- However, nearly one-fifth of patients had below-reference value HRQoL at follow-up
- Intensive care management should take in to consideration follow-up program after intensive care of ICU admitted obstetric patients

ACCEPTED MANUSCRIPT