Correlates of Hormonal Biomarkers with Mental Health and Healthy Behaviors among Mothers of Very-Low-Birthweight Infants

June Cho, PhD, RN
Associate Professor
University of Nevada at Las Vegas
School of Nursing
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Overview

- Maternal mental health is important not only maternal well-being but also infant health and development.
- 13 – 19% of mothers experience psychological problems after birth, esp., mothers of very low birthweight (VLBW, BW < 1,500 gm) infants.
- Mental health problems usually occur within 4 weeks of birth. The first 6 months is a particularly difficult time for mothers with these problems.
- Parenting stress increased more over the first years of life among mothers of VLBW infants than mothers of full-term infants.

Overview

- Measurements of mental health
  - **Self-report** questionnaires
    - Over or under estimation because of social desirability
  - **Biochemical measurements**
    - Testosterone and cortisol
  - **Combining methods**
    - More effective risk identification
- Biomarkers and women's mental health
  - Cortisol levels during pre- and postnatal period
  - Testosterone levels and health-related behaviors
- Measurement of healthy lifestyle behaviors to confirm the direction of the results combining self-report and biochemical measurements

Purpose of the Study

To examine whether;

(1) maternal mental health and healthy behaviors were associated with the levels of testosterone and cortisol over the 2 years at 5 time-points,

(2) maternal healthy behaviors were associated with mental health across 4 time points,

(3) maternal demographic characteristics are associated with the levels of hormonal biomarkers, mental health, and healthy behaviors longitudinally.

Conceptual Framework

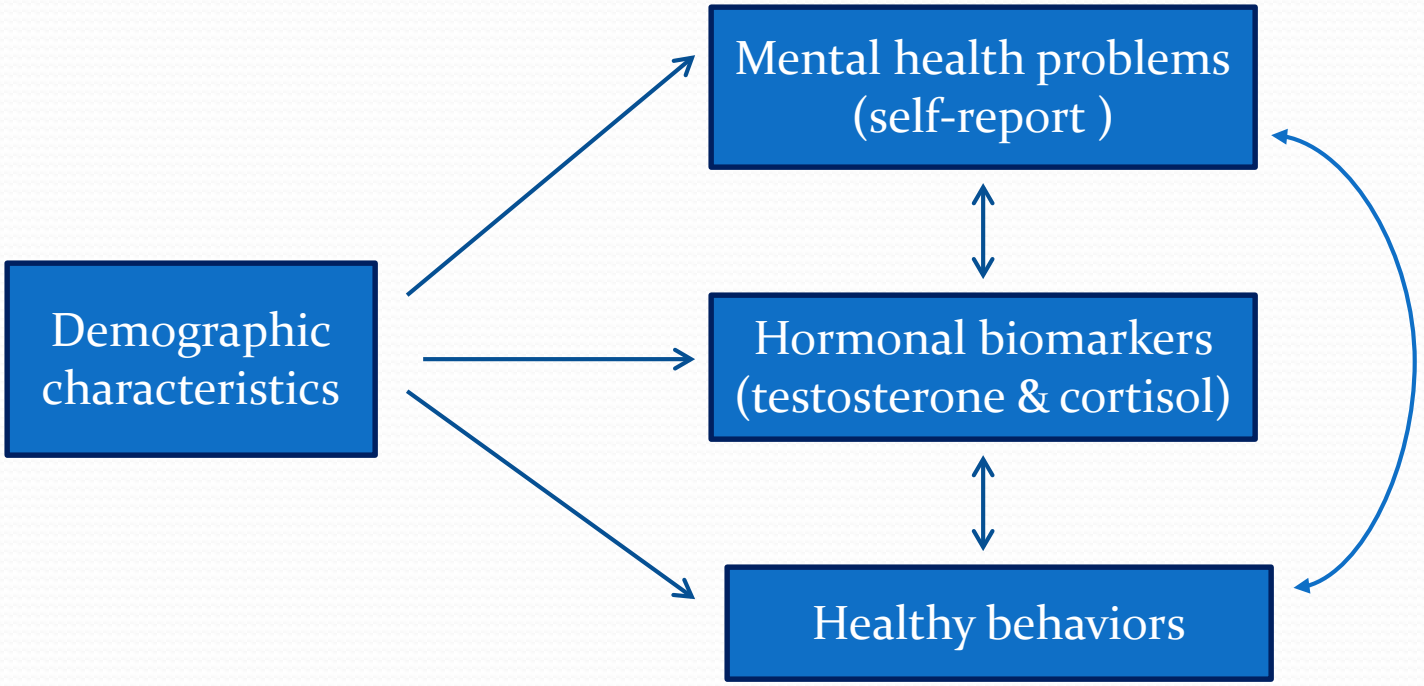

Figure 1. Conceptual Framework for Associations of Hormonal Biomarkers with Mental Health and Healthy Behaviors among Mothers of Very-Low-Birthweight Infants

Samples & Setting

- A convenience sample of **40** mothers of very-low-birthweight (VLBW, BW < 1,500 gm) infants
- Level IV neonatal intensive care unit (NICU) of the University Hospital in the Southeastern US

Eligibility Criteria

- **Inclusion Criteria**
  - Delivery within 7 days
  - 15 years and older
  - Communicate in English
  - To be a primary caregiver of the infant
- **Exclusion Criteria**
  - Dependent on narcotic or injection drugs
  - HIV-positive
  - Serious medical problem such as cancer or psychosis

Measures

- **Maternal mental health**
  - Depressive symptoms (CES-D)
  - Anxiety (STAI/SF)
  - Perceived stress (PSS-10)
  - Parenting stress (PSI-4/SF)
  - Mental health status (SF-12, SFMCS)
  - Healthy behaviors (Lifestyle Index Questionnaire, LIQ)
- **Biochemical measurements**
  - Salivary cortisol
  - Salivary testosterone

Procedure

- University **IRB** approval
- Check the NICU **admission log** on daily basis
- Obtain maternal **consent**
- Review of medical records
- **Self-report questionnaires**
  - The CES-D, STAI/SF, PSS-10 at birth
  - The CES-D, STAI/SF, PSS-10. SF-12, LIQ at 40 weeks PMA
  - The CES-D, STAI/SF, PSS-10, SF-12, LIQ, PSI at 6, 12, & 24 months
- **Biochemical measurements**
  - Using enzyme immunoassay (EIA)
  - Saliva sample collection at 5 times (birth, 40 wks PMA, and 6, 12, and 24 mo)
- **Update maternal demographic information**

Data Analysis

- **Descriptive** statistics
  - For presenting maternal demographic characteristics
- **Mixed linear models**
  - For determining whether maternal T & C levels were associated with maternal mental health & healthy behaviors longitudinally
- Pearson **correlations**
  - For examining correlations between T & C levels at 5 time points

Of the 40 mothers,

- **45**% had more than a high school education
- **30**% were married
- **60**% were African American mothers
- **70**% had a cesarean section
- **60**% had public-assistance health insurance
- Mean maternal age was **26** years
- Mean of gravida and parity were 2.5 and 1.9
- Mean of BMI was **34.3** kg/m^2 at admission to OB & GYN
- **83**% mothers had medical complications during **pregnancy**
  - Gestational hypertension (53%), chorioamnionitis (35%), hypertension prior to pregnancy (18%), diabetes mellitus (8%), antepartum hemorrhage (7%), and use of insulin (5%).
- **100**% of mothers had medical complications at **delivery**
  - Use of steroid (97%), use of antibiotics (95%), and PPROM (53%)

Table 1. Maternal Characteristics and Hormonal Biomarkers

Variable	N	Min	Max	Mean	SD
Age	40	18	38	25.88	5.77
Gravida	40	1	6	2.53	1.40
Parity	40	1	5	1.88	1.07
Race: Caucasian (%)	40			60	
Married (%)	40			45	
Education: < High school (%)	40			45	
Insurance: Public-assistant program (%)	40			60	
Body mass index	40	20.88	49.43	34.26	6.93
Pregnancy complications	40	0	3	1.08	.69
Labor complications	40	2	5	4.43	.81
Prenatal steroid (%)	40			95	
Delivery: Vaginal (%)	40			30	
Testosterone at birth	40	12.65	158.56	64.27	34.33
Cortisol at birth	38	.02	.57	.13	.15
Testosterone at 40 weeks PMA	39	24.99	110.09	52.71	18.87
Cortisol at 40 weeks PMA	39	.04	.58	.23	.12
Testosterone at 6 months	34	26.99	124.62	62.56	23.21
Cortisol at 6 months	34	.07	1.47	.29	.25
Testosterone at 12 months	34	23.43	128.63	55.50	22.02
Cortisol at 12 months	34	.03	.35	.17	.08
Testosterone at 24 months	28	24.19	110.98	55.74	23.07
Cortisol at 24 months	28	.07	.52	.21	.11

Note: Pregnancy complications = number of medical complications during pregnancy, Labor complications = number of medical complications at labor/birth, PMA = postmenstrual age

Table 2. Maternal Mental and Healthy Lifestyle Behaviors over 2 Years after Birth

Variable	N	Min	Max	Mean	SD
Depressive symptoms at birth	40	2	42	13.75	10.23
Depressive symptoms at 40 weeks PMA	38	2	43	13.00	9.69
Depressive symptoms at 6 months	32	1	34	12.13	9.56
Depressive symptoms at 12 months	34	2	43	11.94	9.85
Depressive symptoms at 24 months	30	0	40	13.03	11.22
Perceived stress at birth	40	0	29	14.43	7.56
Perceived stress at 40 weeks PMA	38	0	31	13.39	7.99
Perceived stress at 6 months	32	4	30	13.78	7.26
Perceived stress at 12 months	34	0	34	14.79	6.84
Perceived stress at 24 months	30	0	31	15.13	7.32
Anxiety at birth	40	6	22	10.48	4.10
Anxiety at 40 weeks PMA	38	6	22	9.29	4.11
Anxiety at 6 months	32	6	21	9.31	3.71
Anxiety at 12 months	34	6	17	9.68	3.40
Anxiety at 24 months	30	6	18	9.87	4.04
Mental health status at 40 weeks PMA	38	24.7	65.4	49.13	10.54
Mental health status at 6 months	32	24.7	60.7	48.48	9.53
Mental health status at 12 months	34	25.8	62.5	47.91	9.36
Mental health status at 24 months	30	22.1	63.8	49.95	10.73

Table 2 continued.

Variable	N	Min	Max	Mean	SD
Parenting stress at 6 months	32	36	129	57.34	19.00
Parenting stress at 12 months	34	37	103	62.53	18.04
Parenting stress at 24 months	30	38	117	67.87	22.35
Health behaviors at 40 weeks PMA	38	50.0	96.0	69.40	14.06
Health behaviors at 6 months	31	42.0	95.0	66.32	12.38
Health behaviors at 12 months	34	42.0	95.0	62.65	14.21
Health behaviors at 24 months	30	42.0	94.0	67.57	15.00

Note: PMA = postmenstrual age

Figure 2. CES-D, PSS-10, and STAI/SF at 5 time points (birth, 40 weeks PMA, and 6, 12, and 24 months CA)

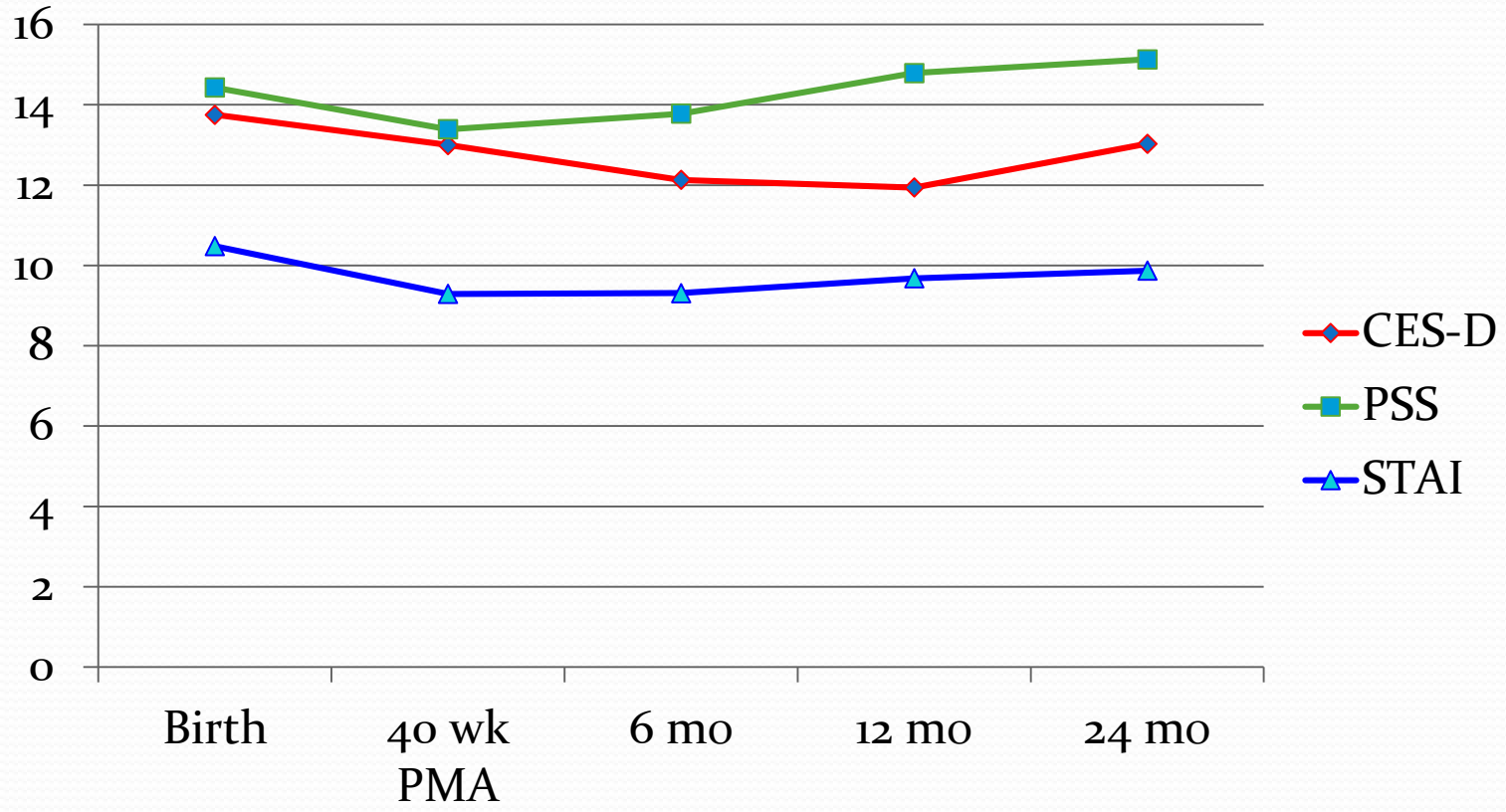

Figure 3. SF-12 (SFMCS), LIQ, PSI-4/SF at 3 - 4 time points (40 weeks PMA, and 6, 12, and 24 months CA)

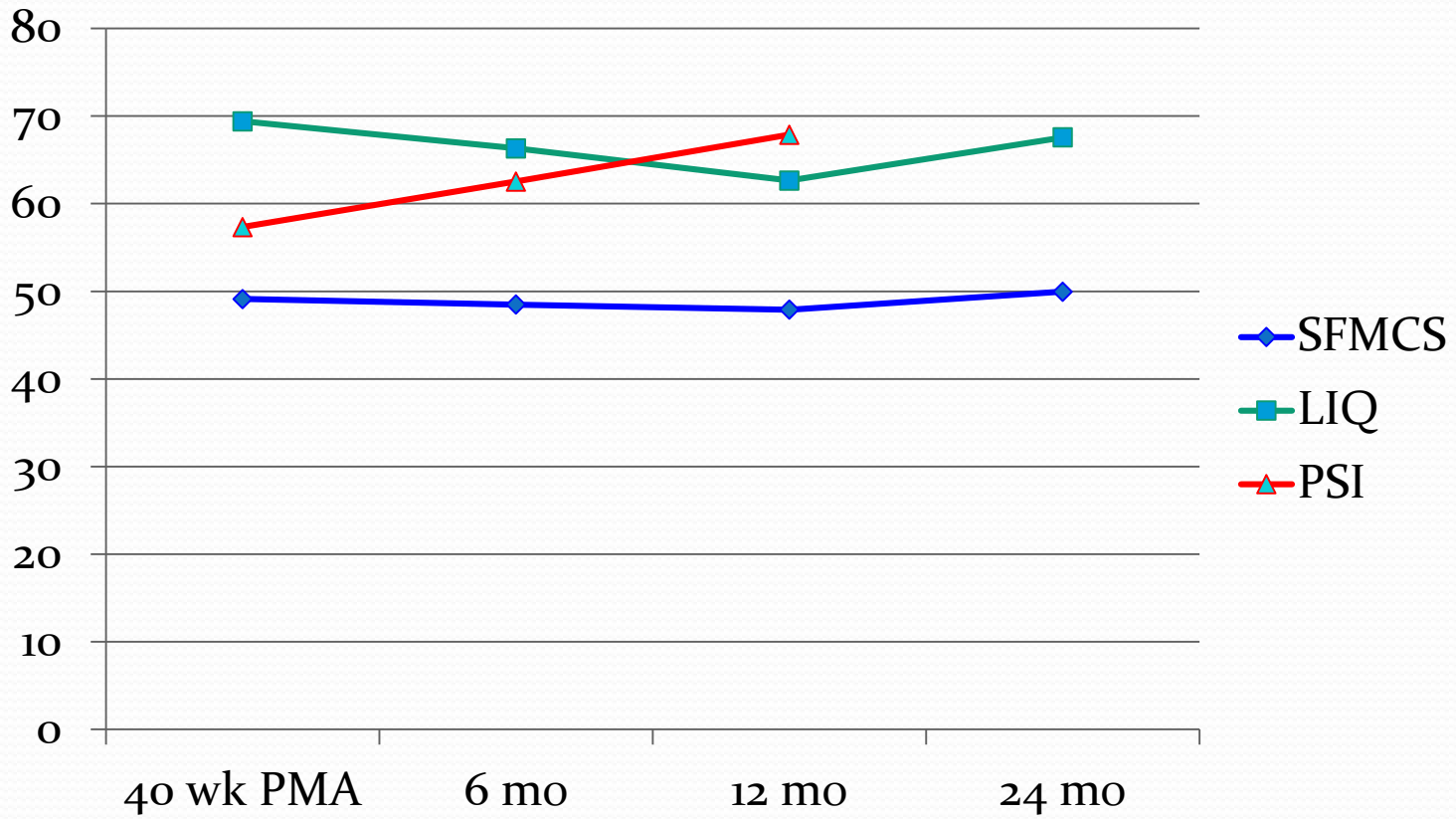

Table 3. Associations of Maternal Hormonal Biomarkers (Testosterone and Cortisol) with Mental Health and Healthy Behaviors over the 2 Years after Birth using Mixed Linear Models

Dependent Variable	Parameter	B	Std. Error	t(df)	Sig.
Depressive symptoms (CES-D)	Testosterone	0.059	.030	1.971(172)	0.05
	Cortisol	4.158	4.722	0.881(169)	0.38
Anxiety (STAI/SF)	Testosterone	0.013	0.012	1.142(172)	0.26
	Cortisol	0.783	1.835	0.427(169)	0.67
Perceived stress (PSS-10)	Testosterone	0.016	0.022	0.708(172)	0.48
	Cortisol	0.026	3.477	0.007(169)	0.99
Mental health status (SFMCS)	Testosterone	-0.026	0.040	-0.655(132)	0.51
	Cortisol	-4.249	5.382	-0.790(132)	0.43
Parenting stress (PSI-4/SF)	Testosterone	0.146	0.090	1.626(94)	0.11
	Cortisol	0.630	11.722	0.054(94)	0.96
LIQ (Healthy eating)	Testosterone	-0.004	0.005	-0.671(124)	0.50
	Cortisol	-1.208	0.723	-1.671(124)	0.10

table continued

Table 3 continued

Dependent Variable	Parameter	B	Std. Error	t	Sig.
LIQ (Physical activity)	Testosterone	0.009	0.051	0.177(131)	0.86
	Cortisol	14.395	6.719	2.142(131)	0.04
LIQ (Current smoking)	Testosterone	-0.031	0.011	-2.774(130)	0.01
	Cortisol	0.330	1.528	0.216(130)	0.83
LIQ (Previous smoking)	Testosterone	-0.017	0.010	-1.821(131)	0.07
	Cortisol	-0.443	1.294	-0.342(131)	0.73
LIQ (Use of alcohol)	Testosterone	0.002	0.007	0.249(128)	0.80
	Cortisol	1.358	0.982	1.383(128)	0.17
LIQ (Total score)	Testosterone	-0.042	0.057	-0.744(131)	0.46
	Cortisol	15.058	7.441	2.024(131)	0.05

Note: CES-D = the Center for Epidemiologic Studies Depression, PSS-10 = Perceived Stress Scale, STAI/SF = State-Trait Anxiety Index, SFMCS = the 12 Item Short Form Health Survey Mental Composite Score, PSI-4/SF = Parenting Stress Index, **LIQ** = Lifestyle Index Questionnaire

Table 4. Associations between Healthy Behaviors and Mental Health over the 2 Years after Birth using Mixed Linear Models

Dependent Variable	Parameter	B	SE	t(df)	Sig.
Depressive symptoms (CES-D)	Healthy eating	-0.522	0.644	-0.810(125)	0.42
	Physical activity	0.030	0.067	0.449(133)	0.65
	Current smoking	0.037	0.304	0.122(132)	0.90
	Previous smoking	-0.623	0.352	-1.767(133)	0.08
	Use of alcohol	-0.636	0.463	-1.373(130)	0.17
Perceived stress (PSS-10)	Healthy eating	-2.207	0.489	-0.423(125)	0.67
	Physical activity	-0.084	0.050	-1.703(133)	0.09
	Current smoking	-0.016	0.226	-0.073(132)	0.94
	Previous smoking	-0.462	0.262	-1.759(133)	0.08
	Use of alcohol	-0.696	0.343	-2.031(130)	0.04
Anxiety (STAI/SF)	Healthy eating	0.133	0.253	0.528(125)	0.60
	Physical activity	-0.002	0.026	-0.080(133)	0.94
	Current smoking	-0.112	0.117	-0.958(132)	0.34
	Previous smoking	-0.427	0.132	-3.232(133)	0.00
	Use of alcohol	-0.255	0.179	-1.426(130)	0.16
Parenting stress (PSI-4/SF)	Healthy eating	-5.010	1.287	-3.893(87)	0.00
	Physical activity	-0.210	0.164	-1.276(95)	0.20
	Current smoking	0.385	0.728	1.147(94)	0.25
	Previous smoking	-1.006	0.861	-1.169(95)	0.24
	Use of alcohol	-2.055	1.054	-1.951(92)	0.06

Table 5. Associations between Demographic Characteristics and Hormonal Biomarkers (Testosterone and Cortisol), Mental Health, and Healthy Behaviors over the 2 Years after Birth using Mixed Linear Models

Variable	Parameter	B	Std. Error	t	Sig.
Testosterone	Marital status	0.190	2.47	0.077(175)	0.94
	Education	-6.412	1.980	-3.238(175)	<0.001
	Insurance	7.773	3.564	2.181(175)	0.03
	Medical complications during pregnancy	7.347	2.786	2.637(175)	0.01
	Race	0.705	3.901	0.181(175)	0.86
	Body mass index	-0.197	0.273	-0.723(175)	0.47
Cortisol	Marital status	0.009	0.016	0.573(172)	0.57
	Education	0.015	0.013	1.124(172)	0.26
	Insurance	0.004	0.023	0.166(175)	0.87
	Medical complications during pregnancy	0.013	0.018	0.733(172)	0.46
	Race	0.002	0.025	0.102(172)	0.92
	Body mass index	0.001	0.002	0.641(172)	0.52
Depressive symptoms	Marital status	5.545	0.893	6.208(174)	<0.001
(CES-D)	Education	-1.946	0.978	-2.439(174)	0.02
	Insurance	4.864	1.392	3.493(174)	<0.001
	Medical complications during pregnancy	-0.425	1.124	-0.378(174)	0.71
	Race	1.376	1.551	0.887(174)	0.38
	Body mass index	-0.019	0.108	-0180(174)	0.86

Table 5 continued.

Variable	Parameter	B	Std. Error	t	Sig.
Perceived stress (PSS-10)	Marital status	2.075	0.709	2.925(174)	<0.001
	Education	-1.346	0.589	-2.286(175)	0.02
	Insurance	1.906	1.051	1.814(175)	0.07
	Medical complications during pregnancy	-0.834	0.826	1.010(174)	0.31
	Race	0.110	1.144	0.096(174)	0.92
	Body mass index	-0.038	0.079	-0.480(174)	0.63
Anxiety (STAI/SF)	Marital status	1.670	0.360	4.634(174)	<0.001
	Education	-6.412	1.980	-3.238(175)	<0.001
	Insurance	1.080	0.551	1.959(174)	0.06
	Medical complications during pregnancy	-0.431	0.434	-0.003(174)	0.32
	Race	1.673	0.588	2.845(175)	0.01
	Body mass index	0.027	0.042	0.646(174)	0.52
Mental health status (SFMCS)	Marital status	-3.897	1.154	-3.378(125)	<0.001
	Education	1.000	0.911	1.098(134)	0.27
	Insurance	-2.427	1.623	-1.495(134)	0.14
	Medical complications during pregnancy	1.540	1.279	1.204(134)	0.23
	Race	-0.686	1.767	-0.389(134)	0.70
	Body mass index	-0.096	0.121	-0.792(134)	0.43

Table 5 continued.

Variable	Parameter	B	Std. Error	t	Sig.
Parenting stress (PSI-4/SF)	**Marital status**	**9.649**	**3.223**	**2.994(96)**	**<0.001**
	Education	**-2.787**	**2.143**	**-1.301(96)**	**0.20**
	Insurance	**7.721**	**3.089**	**2.027(96)**	**0.05**
	Medical complications during pregnancy	**-2.571**	**3.064**	**-0.839(96)**	**0.40**
	Race	**-3.283**	**4.188**	**-0.784(96)**	**0.43**
	Body mass index	**-0.821**	**0.274**	**-2.992(96)**	**<0.001**
Healthy behaviors (LIQ)	**Marital status**	**2.804**	**1.673**	**1.677(133)**	**0.10**
	Education	**-2.966**	**1.272**	**-2.332(133)**	**0.02**
	Insurance	**-0.961**	**2.356**	**-0.408(133)**	**0.68**
	Medical complications during pregnancy	**-4.044**	**1.774**	**-2.280(133)**	**0.02**
	Race	**-0.369**	**2.491**	**-0.148(133)**	**0.88**
	Body mass index	**0.080**	**0.171**	**0.470(133)**	**0.64**

Note: CES-D = the Center for Epidemiologic Studies Depression, PSS-10 = Perceived Stress Scale, STAI/SF = State-Trait Anxiety Index, SFMCS = the 12 Item Short Form Health Survey Mental Composite Score, PSI-4/SF = Parenting Stress Index, **LIQ** = Lifestyle Index Questionnaire

Discussion

- Maternal mental health problems (depressive symptoms, perceived stress, and anxiety) were greatest immediately after birth although the problems decreased from 6 to 12 months after the infant's discharge from the hospital.
- All mental health problems increased at 24 moths including parenting stress. Mental health status measured by SF-12 was worst at 12 months and best at 24 months. This was exactly opposite to the results of other questionnaires.
- The results of maternal mental health problems were inconsistent depending on the **self-report** questionnaires.
- Healthy behaviors were negatively associated with mental health problems
- The results of mental health problems and healthy behaviors using a **biochemical** measurement were consistent throughout the study.

Discussion

- Testosterone levels were negatively associated with maternal mental health and healthy behaviors.
- Cortisol were not related with any maternal mental health problems, but were positively associated with healthy behaviors. This is possibly because of negative correlations between the levels of testosterone and cortisol.
- Testosterone levels could consistently predict maternal mental health and healthy behavior **negatively**, whereas cortisol levels could consistently predict maternal healthy behaviors **positively** during the first years after birth.

Discussion

- Martial status, education, and health insurance were the most **predictive** variables for the levels of hormonal biomarkers, mental health, and healthy behaviors.
- The negative associations of testosterone levels with maternal mental health and healthy behaviors were amplified on considering maternal demographic characteristics.
- Testosterone levels were **higher** in mothers who had less education, more medical complications during pregnancy, and public-assistance health insurance.

Discussion

- In contrast to **other studies**, we found that high testosterone levels are more problematic for maternal mental health and healthy behaviors.
- A systematic literature review using **47 studies** reports that hypercortisolemia is associated with transient depressive status during pregnancy, whereas hypocortisolemia is associated with depressive symptoms during the postpartum period.
- However, we were not able to find those associations between cortisol levels and mental health problems from birth to 24 months.
- Using **both** self-report and biochemical measurement would provide more accurate results needed to understand the nature of mental health problems.

Discussion

- **For future research**
  - Continuing assessment beyond 24 moths is needed as mothers may experience additional parenting difficulties when the infants show more socioemotional and behavioral problems after 24 months
- **For nursing practice**
  - Targeting the assessment of maternal mental health problems using self-report and/or biochemical measurement to the women with greatest risk, e.g., women who are unmarried and have more medical complications during pregnancy, needs to be the focus.

Conclusion

- The use of **combining** self-report and biochemical measurement was found to be effective in assessing maternal mental health and healthy behaviors.
- Testosterone levels were more predictive for maternal mental health and healthy behaviors than cortisol levels.
- The negative associations between testosterone and maternal mental health and healthy behaviors were related with demographic characteristics.
- Assessing problems beyond 24 months is imperative.
- Our findings may provide support for nursing interventions that integrate mental health and healthy behaviors screening into **routine primary care** for mothers who are at risk for poor mental health and parenting difficulties.

Research Team

- June Cho, PhD, RN at UNLV
- Waldemar A. Carlo, MD at UAB
- Kenneth L. McCormick, MD at UAB
- Myriam Peralta, MD at UAB
- Fred Biasini, PhD at UAB
- Xiaogang Su, PhD at UTEP
- Vivien Phillips, BSN, RN at UAB
- Diane Holditch-Davis, PhD, RN, FAAN at Duke University

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