

سطح گلوبولین E در بیماران مبتلای به لنفوسیتوز مزمن (Chronic lymphocytic leukemia, CLL) - مطالعه مقطعی

پستان

مهرنوش پاشایی^{۱*} (M.Sc)، مهدی براتی^{۱+} (M.Sc)، احسان منوچهری دولابی^۵ (M.Sc)، فرحناز قهرمانفرد^۳ (M.D)، مجید میرمحمدخانی^۴ (M.D)، فاطمه پاک^۱ (Ph.D)، پرویز کوخایی^{۵*} (Ph.D)

۱- مرکز تحقیقات سرطان، گروه ایمنولوژی، دانشکده پزشکی، دانشگاه علوم پزشکی سمنان، سمنان، ایران
 ۲- کمیته تحقیقات دانشجویی، دانشگاه علوم پزشکی سمنان، سمنان، ایران
 ۳- گروه پزشکی داخلی، دانشگاه علوم پزشکی سمنان، سمنان، ایران
 ۴- مرکز تحقیقات عوامل اجتماعی موثر بر سلامت، بخش پزشکی اجتماعی، دانشگاه علوم پزشکی سمنان، سمنان، ایران
 ۵- آزمایشگاه ایمنولوژی و ژن‌درمانی، مرکز سرطان کارولینسکا، بیمارستان دانشگاه کارولینسکا، استکهلم، سوئد

چکیده

هدف: این مطالعه گلوبولین E (IgE) را در بیماران مبتلای به لنفوسیتوز مزمن (Chronic lymphocytic leukemia, CLL) مقایسه با افراد سالم انجام داد. روش: این مطالعه مقطعی بود. اهدای خون در این مطالعه در بیماران مبتلای به CLL و افراد سالم انجام شد. سطح IgE در پلاسما، سطح پلاسما، سطح IgE و سطح پلاسما با استفاده از روش ایمنولوژی مقایسه شد. نتایج: سطح IgE در بیماران مبتلای به CLL (۳۷/۱۹±۱۲/۲۱ IU/ml) به طور معنی‌داری بالاتر از افراد سالم (۹/۰۴±۴/۲۶ IU/ml) بود. سطح IgE در بیماران مبتلای به CLL به طور معنی‌داری بالاتر از افراد سالم بود. نتیجه: سطح IgE در بیماران مبتلای به CLL به طور معنی‌داری بالاتر از افراد سالم بود.

روش: این مطالعه مقطعی بود. اهدای خون در این مطالعه در بیماران مبتلای به CLL و افراد سالم انجام شد. سطح IgE در پلاسما، سطح پلاسما، سطح IgE و سطح پلاسما با استفاده از روش ایمنولوژی مقایسه شد. نتایج: سطح IgE در بیماران مبتلای به CLL (۳۷/۱۹±۱۲/۲۱ IU/ml) به طور معنی‌داری بالاتر از افراد سالم (۹/۰۴±۴/۲۶ IU/ml) بود. سطح IgE در بیماران مبتلای به CLL به طور معنی‌داری بالاتر از افراد سالم بود. نتیجه: سطح IgE در بیماران مبتلای به CLL به طور معنی‌داری بالاتر از افراد سالم بود.

نتیجه: سطح IgE در بیماران مبتلای به CLL به طور معنی‌داری بالاتر از افراد سالم بود. نتیجه: سطح IgE در بیماران مبتلای به CLL به طور معنی‌داری بالاتر از افراد سالم بود.

کلیدی: گلوبولین E، لنفوسیتوز مزمن (CLL)، سرطان، ایمنولوژی

مقدمه

لنفوسیت‌های B توموری با افزایش بیان مارکرهای تمایزی CD5، CD20، CD19، CD23 و بیان کم ایمنوگلوبولین‌های غشایی (IgM و IgD) در خون محیطی، مغز استخوان، غدد لنفاوی و طحال همراه است. این بیماری در افراد بالغ با

لنفوسیتوز مزمن (Chronic lymphocytic leukemia, CLL) یکی از شایع‌ترین بدخیمی‌های خونی در کشورهای غربی است، که با تکثیر منوکلونال و تجمع

این تومورها است [۱۴]. در برخی دیگر از مطالعات آینده‌نگر نیز سطح بالای IgE، خطر ابتلا به بیماری لوسمی لنفوسیتی مزمن را کاهش می‌دهد [۱۵]. در مطالعات اپیدمیولوژیکی در غالب متآنالیز رابطه‌ای میان سابقه بیماری‌های آلرژی از جمله آسم، تب یونجه و خطر ابتلا به سرطان پستان در جمعیت زنان کانادایی مبتلا به سرطان پستان مشاهده نشده است [۱۶]. یافته‌های مطالعات اخیر در زمینه‌ی آلرژی-انکولوژی و وجود سابقه بیماری‌های آلرژی و سطح IgE در سرم خون محیطی، با ابتلا به برخی سرطان‌ها مرتبط است و در استفاده از IgE به عنوان ایمونوتراپی علیه تومورها موثر است [۱۷]. لذا ارزیابی سطح پلاسمایی IgE در دو نوع سرطان شایع از جمله بیماران مبتلا به لوسمی لنفوسیتی مزمن و بیماران مبتلا به سرطان پستان نسبت به افراد کنترل از اهداف این مطالعه است.

مواد و روش‌ها

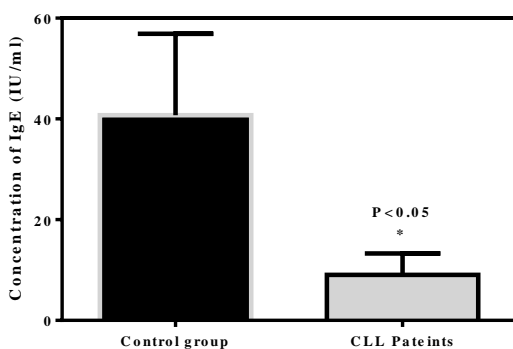
نه‌گیری. نمونه‌های خون محیطی توسط ونوجکت حاوی ضدانعقاد هپارین از ۲۰ بیمار مبتلا به لوسمی لنفوسیتی مزمن در آزمایشگاه تشخیص طبی بیمارستان کوثر استان سمنان جمع‌آوری گردید. از جمله ویژگی‌های این بیماران محدوده‌ی سنی ۷۰-۴۰ سال با محدوده‌ی لکوسیتی $10^3 \times 5/60 - 1/10$ و دارای ۹۰-۶۰ درصد لنفوسیت بود. بررسی بیماران توسط انکولوژیست و برطبق دستورالعمل‌های بین‌المللی معیارهای تشخیصی لوسمی لنفوسیتی مزمن صورت گرفت [۱۸]. نمونه‌های جمع‌آوری شده در فازهای اولیه و متوسط بیماری بر اساس رتبه‌بندی سیستم Rai و سیستم Binet قرار گرفته بودند و بیماری CLL در نمونه‌های جمع‌آوری شده از نوع غیرپیش‌رونده بود [۱۹،۲۰]. هم‌چنین ۲۰ نمونه‌ی خون محیطی از افراد مبتلا به سرطان پستان در آزمایشگاه تشخیص طبی بیمارستان کوثر در استان سمنان جمع‌آوری گردید. از جمله ویژگی‌های این بیماران محدوده‌ی سنی ۸۰-۳۵ سال، در مرحله‌ی ۰ / ۱ A / ۲ A و ۳ A و از نوع خوش‌خیم و بدخیم بود. پرونده‌ی بیماران هم افراد مبتلا به لوسمی لنفوسیتی مزمن و هم افراد مبتلا به سرطان پستان از

میانگین سنی ۶۵ سال شناسایی می‌گردد [۱،۲]. در سال ۲۰۰۸ در ایالات متحده به‌طور تقریبی ۱۵۱۱۰ مورد جدید بیمار مبتلا به لوسمی لنفوسیتی مزمن شناسایی گردید، که ۴۳۹۰ نفر همراه با بیماری مذکور جان خود را از دست دادند [۳]. در میان سرطان‌های شایع، سرطان پستان از جمله شایع‌ترین انواع سرطان در بین زنان کشورهای درحال توسعه و توسعه‌یافته می‌باشد. به‌طور تقریبی ۱/۴ میلیون زن مبتلا به سرطان پستان در سراسر جهان، در سال ۲۰۰۸ شناسایی گردید و ۴۵۹/۰۰۰ نفر توسط این بیماری جان خود را از دست دادند [۴]. مطالعات اپیدمیولوژیک متعددی به منظور مشخص کردن رابطه‌ی واکنش‌های آلرژی و ریسک ابتلا به انواع سرطان، صورت گرفته است. در واکنش‌های آلرژی برخی فاکتورهایی همانند ایمونوگلوبولین E آزاد شده که منجر به افزایش پاسخ‌های ضد توموری می‌گردد، با این وجود روند شیوع بیماری‌های آلرژی رو به افزایش است، این در حالی است که حدود ۴۰٪ جمعیت غرب دارای علائم اتوبی هستند، که به معنی تولید بیش از حد IgE به انواع آلرژن‌ها است [۵،۶]. ایمونوگلوبولین E، در پاسخ به عفونت‌های انگلی کرمی و تک یاخته‌ای تولید می‌گردد [۷-۹] و در بروز پاسخ‌های ازدیاد حساسیت نوع ۱ دارای نقشی کلیدی است، به گونه‌ای که در بروز برخی بیماری‌های آلرژیک مانند آسم، آلرژی‌های غذایی و رینیت آلرژیک دارای نقش است [۱۰-۱۲]. پس از آغاز مطالعات بحث‌برانگیز اپیدمیولوژی در ارتباط میان سرطان و استعداد آلرژی، زمینه‌ی تحقیقات به منظور آشکارسازی عمل‌کرد پاسخ‌های ایمنی به واسطه‌ی IgE علیه سرطان آغاز گردید. مطالعات نشان‌دهنده‌ی این بود که آنتی‌بادی IgE، در مراقبت ایمنی علیه تومور و هم‌چنین در ایمونوتراپی‌های فعال و غیرفعال موثر می‌باشد و به عنوان یک آنتی‌بادی ضد توموری در پاسخ به تومورها دارای نقش است [۱۳]. از سوی دیگر، مطالعات اپیدمیولوژی صورت گرفته نیز نشان‌دهنده‌ی یک ارتباط معکوس بین سطح پلاسمایی IgE و خطر ابتلا به لوسمی در دوران کودکی، گلیوما، سرطان پانکراس است و بیانگر عمل‌کرد ضد توموری IgE در ایمنی

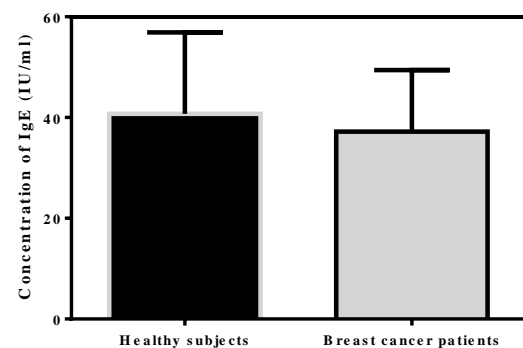
بیمارستان کوثر سمنان مراجعه نموده بودند، نسبت به افراد سالم به طور قابل توجهی کم تر بود (شکل ۱). در حالی که بین سطح IgE اندازه گیری شده در پلاسماهای افراد سالم و سرم افراد مبتلا به سرطان پستان هیچ تفاوت معنی داری ملاحظه نشد (شکل ۲).

در یافته های پژوهش میانگین سطح پلاسمایی IgE در افراد مبتلا به لوسمی لنفوسیتی مزمن $9/045 \pm 4/261$ IU/ml و در افراد کنترل $40/73 \pm 16/18$ IU/ml بود و از نظر آماری اختلاف معنی داری بین دو گروه مورد و شاهد مشاهده شد (جدول ۱).

در یافته های پژوهش میانگین سطح پلاسمایی IgE در افراد مبتلا به سرطان پستان $37/19 \pm 12/21$ و در افراد کنترل $40/73 \pm 16/18$ IU/ml بود و از نظر آماری اختلاف معنی داری بین دو گروه مورد و شاهد مشاهده نشد (جدول ۲).



شکل ۱. مقایسه سطح IgE پلاسمایی در نمونه های اخذ شده از افراد بیمار مبتلا به لوسمی لنفوسیتی مزمن و گروه کنترل. سطح IgE در افراد بیمار نسبت به گروه کنترل بطور قابل توجهی کمتر است ($P=0.0111$)



شکل ۲. مقایسه سطح IgE پلاسمایی در نمونه های اخذ شده از افراد بیمار مبتلا به سرطان پستان و گروه کنترل. بین سطح IgE در افراد بیمار و گروه کنترل تفاوت معنی داری مشاهده نشد ($P=0.4305$)

نظر عدم سابقه بیماری های آلرژیک و انگلی، هم چنین عدم مصرف درمان های مربوط به لوسمی لنفوسیتی مزمن و درمان مربوط به سرطان پستان از قبیل شیمی درمانی، رادیوتراپی و ایمونوتراپی را در ۲ سال اخیر و عدم مصرف داروهای جانبی از جمله داروهای سرکوب کننده سیستم ایمنی در یک هفته گذشته مورد بررسی قرار گرفتند.

هم چنین ۲۰ نمونه ی خون محیطی از افراد سالم منطبق شده با سن بیماران به عنوان گروه کنترل جمع آوری گردید. تهیه ی نمونه خون از افراد بیمار مبتلا به لوسمی لنفوسیتی مزمن، افراد مبتلا به سرطان پستان و افراد سالم پس از دریافت رضایت نامه آگاهانه که بر اساس کمیته اخلاق دانشگاه علوم پزشکی سمنان تهیه گردیده بود، صورت گرفت.

آماده سازی پلاسمای: نمونه های خون محیطی تهیه شده از هر فرد را با سرعت ۳۰۰۰ دور در دقیقه به مدت ۱۰ دقیقه سانتریفیوژ نموده، پس از جداسازی، پلاسمای دریافتی را در فریزر 80°C به منظور بررسی سطح آنتی بادی، قرار گرفت. اندازه گیری آنتی بادی توسط الایزا: سطح ایمونوگلوبولین E در نمونه های پلاسمایی جمع آوری شده را توسط روش الایزا (Enzyme linked immunsorbent assay, ELISA) بر طبق دستورالعمل کیت های تجاری موجود (کیت الایزای سنجش IgE، شرکت پادتن علم Lot no: IgE 0515) و توسط دستگاه الایزایدر (SPECTRA III-Germany) مورد سنجش قرار گرفت (حداقل غلظت قابل سنجش کیت سنجش IgE 1IU/ml و حداکثر اختصاصیت بالای ۹۹ درصد برای IgE انسانی).

آنالیز آماری: تجزیه تحلیل آماری با استفاده از آزمون کولموگراف اسمیرنوف، در صورت نرمال بودن داده ها تست t زوجی در سطح معنی داری ۰/۰۵ با استفاده از نرم افزار spss نسخه ۱۶ انجام شد.

نتایج

نتایج حاصل از پژوهش مشخص نمود که سطح IgE در پلاسماهای افراد مبتلا به لوسمی لنفوسیتی مزمن، که به

جدول ۱. شاخص آماری سطح IgE در پلاسما افراد مبتلا به لوسمی لنفوسیتی مزمن در مقایسه با افراد سالم

شاخص آماری			گروه‌ها
P-value	انحراف معیار از میانگین Mean ±SEM	تعداد	
p < 0.01	۹۰,۴۵±۴,۲۶۱	۲۰	گروه مورد (لوسمی لنفوسیتی مزمن)
	۴۰,۷۳±۱۶,۱۸	۲۰	گروه کنترل

جدول ۲. شاخص آماری سطح IgE در سرم افراد مبتلا به سرطان پستان در مقایسه با افراد سالم

شاخص آماری			گروه‌ها
P-value	انحراف معیار از میانگین Mean ±SEM	تعداد	
p > 0.4	۳۷,۱۹±۱۲,۲۱	۲۰	گروه مورد (سرطان پستان)
	۴۰,۷۳±۱۶,۱۸	۲۰	گروه کنترل

بحث و نتیجه‌گیری

آنتی‌بادی IgE یکی از انواع آنتی‌بادی‌ها است که شواهد نشان می‌دهد که تجمع این آنتی‌بادی در برخی بدخیمی‌ها اثر حفاظتی دارد و در ایمنی ضد تومور دارای نقش است. غلظت IgE در سرم افراد نرمال پایین (به‌طور تقریبی ۳۰ ng/ml) است. اما غلظت این آنتی‌بادی در بیماری‌های آلرژیک و عفونت‌های انگلی افزایش می‌یابد [۲۱]. در واکنش‌های آلرژیک که عواملی مانند IgE تولید می‌گردد، در ریسک ابتلا به برخی سرطان‌های خونی تاثیرگذار است. مطالعات اپیدمیولوژیک و متاآنالیزهای گسترده‌ای انجام گرفته است که نشان‌دهنده‌ی رابطه‌ی معکوس بین استعداد آلرژیک و ریسک ابتلا به برخی سرطان‌ها از جمله گلیوما، لوسمی در دوران کودکی (لوسمی لنفوبلاستیک حاد) است [۱۴]. اما در برخی سرطان‌های دیگر از جمله سرطان ریه، سرطان پروستات و سرطان مثانه وجود استعداد آلرژیک و بروز سرطان به‌طور معنی‌داری با یکدیگر رابطه‌ی مستقیم دارند، در حالی‌که سرطان‌های دیگری از جمله سرطان پستان، سرطان تخمدان و سرطان رحم بین آلرژیک و خطر ابتلا به سرطان رابطه معناداری دیده نشده است [۲۲]. هم‌چنین مطالعه‌ای جهت مشخص نمودن ارتباط مارکر بیولوژی در بیماری اتوپی و خطر ابتلا به سرطان پروستات، سرطان پستان، سرطان ریه و سرطان

کلورکتال انجام گرفت، هیچ رابطه‌ی معنی‌داری در خطر ابتلا به سرطان پستان مشاهده نشده است [۲۳]. در مطالعات اخیر که در سال ۲۰۱۶ صورت گرفت، مشخص شده است بیمارانی که مستعد ابتلا به بیماری‌های آلرژیک هستند و به تازگی به سرطان پستان مبتلا گردیدند، سطح IgE پلاسمایی بیماران مبتلا به سرطان پستان که در گذشته مبتلا به واکنش‌های ازدیاد حساسیت تیپ ۱ بودند و جمعیت سالم، به‌طور مشابه است و ارتباطی میان ابتلا به سرطان پستان و انواع آلرژیک تیپ ۱ وجود ندارد [۲۴]. در مطالعه‌ی حاضر نشان داده شده است که ارتباط بین سطح IgE و سرطان پستان هم‌چنان نامعلوم است. تفاوتی میان سطح پلاسمایی IgE در افراد نرمال و افراد مبتلا به سرطان پستان که سابقه‌ی بیماری‌های انگلی و آلرژیک ندارند، مشاهده نشده است.

اما مطالعه‌ی اپیدمیولوژیکی که در سال ۲۰۱۵ صورت گرفته است نشان می‌دهد که سطح پایین IgE، خطر ابتلا به بیماری لوسمی لنفوسیتی مزمن را افزایش می‌دهد، اما تایید این نتیجه نیاز به اطلاعات ایمونولوژی دقیق است [۱۵]. همان‌گونه که یافته‌های ایمونولوژی در مطالعه‌ی ما، نشان می‌دهد که در افراد مبتلا به لوسمی لنفوسیتی مزمن سطح پایین‌تری از ایمونوگلوبین E نسبت به افراد کنترل قابل سنجش است. در این مطالعه مشخص گردید که افرادی که

سلول‌های لنفوسیتی افراد مبتلا به CLL این مولکول را به میزان بالایی بیان می‌کنند.

از سوی دیگر سطح IgE در سرم افراد به‌طور قوی متأثر از مواجهه با فاکتورهای محیطی است، اما برخی عوامل از جمله سلول‌های TCD4⁺ و بیان برخی ژن‌ها توسط این سلول‌ها به عنوان مثال گیرنده‌ی IL-17RB در میزان سطح پلاسمایی IgE ایفای نقش می‌نمایند. گیرنده‌ی IL-17RB بر روی سلول‌های TCD4⁺ قرار گرفته و گیرنده‌ی دو سایتوکاین از خانواده IL-17 که عبارتند از IL-17B و با میل ترکیبی بالاتر به IL-17E است. اتصال IL-17RB به IL-17E منجر به افزایش شدت بیماری آسم، تولید الگوی سایتوکاینی Th2 و افزایش سطح IgE می‌گردد. در برخی مطالعات ارتباط مستقیم قوی بین میزان بیان گیرنده‌ی IL-17RB بر سطح لنفوسیت‌های TCD4⁺ به ویژه در مردان و افزایش میزان سطح پلاسمایی IgE مشخص شده است [۲۸]. بنابراین ممکن است یکی از دلایل کاهش سطح پلاسمایی IgE در لوسمی لنفوسیتی مزمن کاهش سطح IL-17E در سرم و کاهش بیان گیرنده‌ی IL-17RB بر سطح سلول‌های TCD4⁺ باشد. بر طبق یافته‌های به دست آمده سطح IgE موجود در پلاسمای افراد مبتلا به لوسمی لنفوسیتی مزمن پایین‌تر از افراد گروه نرمال می‌باشد ولی این تفاوت معنی‌داری بین گروه کنترل و افراد مبتلا به سرطان پستان مشاهده نشده است. با توجه به نقش ضد توموری IgE و سطح پایین این ایمونوگلوبولین در پلاسمای افراد مبتلا به لوسمی لنفوسیتی مزمن به نظر می‌رسد که یک راه‌کار درمانی موثر و غیرشیمیایی، استفاده از این مولکول بیولوژیک ایمنی باشد؛ هم‌چنین در افراد مبتلا به بیماری‌های آلرژیک پاسخ سیستم ایمنی علیه برخی تومورها از جمله لوسمی لنفوسیتی مزمن می‌تواند با شدت بیش‌تری صورت گیرد. که مطالعات بیش‌تر در این زمینه را می‌طلبد. با توجه به این‌که این مطالعه تنها بر روی سطح پلاسمایی IgE در بیماران مبتلا به لوسمی لنفوسیتی مزمن و سرطان پستان صورت گرفته است و فاکتورهای موثر بر سطح IgE در سرم دو بیماری مذکور از جمله سطح CD23 محلول و سطح IL-

سطح IgE کم‌تری از ۲۴/۵۵ IU/ml دارند، مستعد ابتلا به لوسمی لنفوسیتی مزمن هستند. آنتی‌بادی IgE به سلول‌های اجرایی از طریق دو گروه گیرنده متصل می‌گردد، عبارتند از Fcε RI، با میل پیوندی بالا نسبت به IgE، که بر روی ماست سل‌ها، بازوفیل‌ها، ائوزینوفیل‌ها حضور دارد که در ایجاد واکنش‌های ازدیاد حساسیت نوع یک ایفای نقش می‌کنند، و CD23 یا Fcε RII که یک گیرنده‌ی با میل پیوندی پایین برای IgE است، که به‌طور عمده بر روی لنفوسیت‌های B بیان می‌گردد. مارکر CD23 در برخی بیماری‌ها بر روی سلول‌ها به میزان بالایی بیان می‌گردد. در لوسمی لنفوسیتی مزمن بر سطح سلول‌های توموری، مارکر تمایزی CD23 که گیرنده‌ی با میل ترکیبی پایین برای IgE است و مولکولی جهت تنظیم تولید IgE به‌صورت تنظیم فیدبک منفی است، به میزان فزونی بیان می‌گردد؛ مهار و یا فقدان CD23 منجر به افزایش غیرطبیعی سطح پلاسمایی IgE و بالعکس می‌گردد [۲۵]. اتصال IgE یا آنتی‌بادی مونوکلونال علیه CD23، تکثیر و تمایز لنفوسیت‌های B و هم‌چنین تولید IgE را مهار می‌نماید [۲۶]، مولکول غشایی CD23 بر اثر پروتازهای موجود در داخل غشا شکسته شده و به شکل CD23 محلول تبدیل می‌گردد. اتصال فرم محلول CD23 به مولکول CD21 (گیرنده‌ی کمپلمان) و IgE غشایی منجر به افزایش تولید IgE می‌گردد. اما اتصال IgE به مولکول CD23 غشایی مانع از شکست CD23 شده و تولید CD23 محلول و تحریک سنتز IgE را مهار می‌کند [۲۵]. احتمال می‌رود به دلیل بیان بیش از حد CD23 بر روی سلول‌های توموری در لوسمی لنفوسیتی مزمن باعث اتصال IgE به CD23 شده و مانع از تشکیل فرم محلول CD23 می‌گردد و متعاقب آن سطح IgE پلاسمایی کاهش می‌یابد. بر اساس تئوری "فرار تومور" (Tumor escape) سلول‌های توموری با کاهش سطح عوامل مهارکننده‌ی رشد تومور شرایط را برای رشد و پیشرفت تومور فراهم می‌کنند [۲۷]، مکانیسم کاهش سطح IgE پلاسمایی از طریق پیام‌رسانی منفی مولکول غشایی CD23 می‌باشد که

Omalizumab, an anti-IgE antibody, in the treatment of adults and adolescents with perennial allergic rhinitis. *Ann Allergy Asthma Immunol* 2003; 91: 160-167.

[13] Nigro EA, Siccardi AG, Vangelista L. Role and Redirection of IgE against Cancer. *Antibodies* 2013; 2: 371-391.

[14] Jensen-Jarolim E, Achatz G, Turner M, Karagiannis S, Legrand F, Capron M, Penichet M, Rodriguez J, Siccardi A, Vangelista L. AllergoOncology: the role of IgE-mediated allergy in cancer. *Allergy* 2008; 63: 1255-1266.

[15] Helby J, Bojesen SE, Nielsen SF, Nordestgaard BG. IgE and risk of cancer in 37 747 individuals from the general population. *Annals of oncology: official journal of the European Society for Medical Oncology / ESMO* 2015; 26: 1784-1790.

[16] Lowcock EC, Cotterchio M, Ahmad N. Association between allergies, asthma, and breast cancer risk among women in Ontario, Canada. *Cancer Causes Control* 2013; 24: 1053-1056.

[17] Singer J, Jensen-Jarolim E. IgE-based immunotherapy of cancer: challenges and chances. *Allergy* 2014; 69: 137-149.

[18] Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Dohner H, Hillmen P, Keating MJ, Montserrat E, Rai KR, Kipps TJ. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute-Working Group 1996 guidelines. *Blood* 2008; 111: 5446-5456.

[19] Kokhaei P, Palma M, Mellstedt H, Choudhury A. Biology and treatment of chronic lymphocytic leukemia. *Ann Oncol* 2005; 16: ii113-123.

[20] Keating MJ, Chiorazzi N, Messmer B, Damle RN, Allen SL, Rai KR, et al. Biology and treatment of chronic lymphocytic leukemia. *Hematology Am Soc Hematol Educ Program* 2003; 2003: 153-175.

[21] Riemer AB, Untersmayr E, Knittelfelder R, Duschl A, Pehamberger H, Zielinski CC, Scheiner O, Jensen-Jarolim E. Active induction of tumor-specific IgE antibodies by oral mimotope vaccination. *Cancer Res* 2007; 67: 3406-3411.

[22] Turner MC, Chen Y, Krewski D, Ghadirian P. An overview of the association between allergy and cancer. *Int J Cancer* 2006; 118: 3124-3132.

[23] Wang H, Rothenbacher D, Low M, Stegmaier C, Brenner H, Diepgen TL. Atopic diseases, immunoglobulin E and risk of cancer of the prostate, breast, lung and colorectum. *Int J Cancer* 2006; 119: 695-701.

[24] Zhang H, Guo G, Jianzhong C, Zheng Y. Decreased Level of IgE is Associated with Breast Cancer and Allergic Diseases. *Med Sci Monit* 2016; 22: 587-597.

[25] Hibbert RG, Teriete P, Grundy GJ, Beavil RL, Reljic R, Holers VM, et al. The structure of human CD23 and its interactions with IgE and CD21. *J Exp Med* 2005; 202: 751-760.

[26] Luo H, Hofstetter H, Banchereau J, Delespesse G. Cross-linking of CD23 antigen by its natural ligand (IgE) or by anti-CD23 antibody prevents B lymphocyte proliferation and differentiation. *J Immunol* 1991; 146: 2122-2129.

[27] Pak F, Barati M, Shokrolahi M, Kokhaei P. Tumor immunology and tumor escape mechanisms from immune response. *Koomesh* 2014; 15: 412-430. (Persian).

[28] Hunninghake GM, Chu JH, Sharma SS, Cho MH, Himes BE, Rogers AJ, et al. The CD4+ T-cell transcriptome and serum IgE in asthma: IL17RB and the role of sex. *BMC Pulm Med* 2011; 11: 17.

17RB در سطح سلول‌های TCD4⁺ سنجیده نشده است،

پیشنهاد می‌شود در مطالعات آینده عوامل موثر بر آزادسازی

IgE نیز مورد بررسی قرار گیرد.

تشکر و قدردانی

تشکر از حمایت معاونت محترم حقیقات و فناوری

دانشگاه علوم پزشکی سمنان که ما را در انجام پژوهش فوق و

تدوین این مقاله پشتیبانی نمودند.

منابع

[1] Chiorazzi N, Rai KR, Ferrarini M. Chronic lymphocytic leukemia. *N Engl J Med* 2005; 352: 804-815.

[2] Moshfeghi K, Mosayebi G. Therapeutic effects of fludarabine-cyclophosphamide combined therapy in Iranian patients with B-cell chronic lymphocytic leukemia. *Koomesh* 2015; 16: 202-206.

[3] Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. *CA Cancer J Clin* 2009; 59: 225-249.

[4] Youlden DR, Cramb SM, Dunn NA, Muller JM, Pyke CM, Baade PD. The descriptive epidemiology of female breast cancer: an international comparison of screening, incidence, survival and mortality. *Cancer Epidemiol* 2012; 36: 237-248.

[5] Van Hemelrijck M, Garmo H, Binda E, Hayday A, Karagiannis SN, Hammar N, Walldius G, Lambe M, Jungner I, Holmberg L. Immunoglobulin E and cancer: a meta-analysis and a large Swedish cohort study. *Cancer Causes Control* 2010; 21: 1657-1667.

[6] Martínez-Maza O, Moreno AD, Cozen W. Epidemiological evidence: IgE, allergies, and hematopoietic malignancies. *Cancer and IgE: Springer*; 2010. p. 79-136.

[7] Gurish MF, Bryce PJ, Tao H, Kisselgof AB, Thornton EM, Miller HR, Friend DS, Oettgen HC. IgE enhances parasite clearance and regulates mast cell responses in mice infected with *Trichinella spiralis*. *J Immunol* 2004; 172: 1139-1145.

[8] Walter K, Fulford AJ, McBeath R, Joseph S, Jones FM, Kariuki HC, Mwatha JK, Kimani G, Kabatereine NB, Vennervald BJ. Increased human IgE induced by killing *Schistosoma mansoni* in vivo is associated with pretreatment Th2 cytokine responsiveness to worm antigens. *J Immunol* 2006; 177: 5490-5498.

[9] Vouldoukis I, Mazier D, Moynet D, Thiolat D, Malvy D, Mossalayi MD. IgE mediates killing of intracellular *Toxoplasma gondii* by human macrophages through CD23-dependent, interleukin-10 sensitive pathway. *PLoS One* 2011; 6: e18289.

[10] Gould HJ, Sutton BJ, Beavil AJ, Beavil RL, McCloskey N, Coker HA, Fear D, Smurthwaite L. The biology of IgE and the basis of allergic disease. *Annual Rev Immunol* 2003; 21: 579-628.

[11] Gould HJ, Sutton BJ. IgE in allergy and asthma today. *Nature Rev Immunol* 2008; 8: 205-217.

[12] Chervinsky P, Casale T, Townley R, Tripathy I, Hedgecock S, Fowler-Taylor A, Shen H, Fox H.

Review Article

The quality of life in cancer patients in Iran: A systematic review by using meta-analysis

Diana Saroukhani (M.Sc)¹, Khadijeh Omid (M.Sc)¹, Reza Norouzi (M.Sc)², Hakimeh Zali (Ph.D)^{*2}, Kourosh Sayehmiri (Ph.D)¹, Mohammad Forozeshfard (M.D)³

1 - Psychological Injuries Research Center, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran

2 - Proteomics Research Center, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3 - Cancer Research Center, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran

(Received: 9 Jul 2015; Accepted: 26 May 2016)

Introduction: Cancer is the third leading cause of death after cardiovascular diseases and accidents. Patients with cancer do not have a good quality of life. Therefore, the purpose of this study was investigating the state of quality of life in cancer patients in Iran, using the meta-analysis method.

Materials and Methods: The search was done using keywords: Quality of Life, Cancer and Iran in the foreign databases of Pubmed, Scopus, Medline, ISI, Google Scholar and native databases such as Sid, Medlib, Iranmedex and Magiran. Data was analyzed using meta-analysis (Random Effects Model). The heterogeneity of the studies was investigated using I² index. Data was analyzed using STATA Ver.11 software. SF-36, E-Q-C-30, TNO-AZL, WB-26, BR23-C 30 and QOL-BC questionnaires were used in the investigations.

Results: Among the 17 accomplished studies in Iran with the sample size of 1476 from year 2003 to 2015, the average quality of life score for cancer patients in Iran was 42 (confidence interval 95%: 34.05 to 49.96) and in men and women were 28.90 and 30.61, respectively. The average quality of life score for the emotional aspect were 55.20, social 40.8, mental health 36.50, physical health 38.17, respectively. The prevalence of quality of life as good, fair and bad were 47%, 34% and 9%, respectively.

Conclusion: The average quality of life score of cancer patients is higher in women in compare to men.

Keywords: Quality of Life, Neoplasms, Iran, Meta-Analysis

* Corresponding author. Tel: +98 21 22439848

h.zali@sbmu.ac.ir

Expression of CD86 Co-stimulatory gene in colon polyps

Noshad Peyravian (M.Sc)¹, Hamid Asadzadeh (M.D)^{*2}, Ehsan Nazemalhosseini Mojarad (Ph.D)³, Mehrdad Hashemi (Ph.D)⁴, Mohammadreza Razavi (M.Sc)⁵

1- Dept. of Molecular and Cellular Sciences, Faculty of Advanced Sciences and Technology, pharmaceutical Sciences Branch, Islamic Azad University, Tehran, Iran (IAUPS)

2- Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Centre, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3 - Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

4- Dept. of Genetics, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran

5 - Nursing Care Research Center, Student Research Committee, Semnan University of Medical Sciences, Semnan, Iran

(Received: 25 Oct 2015; Accepted: 30 Apr 2016)

Introduction: Since the majority of colorectal cancers originate from polyps in the area, therefore, the investigation of the immunological gene expression in colon polyps can be used as a factor for the detection of genetic and pathological differences in polyps. The aim of this study was investigating the expression of CD86 gene in colorectal polyps and its association with malignancy.

Materials and Methods: In a descriptive-analytical study during (2012 to 2014), forty-nine biopsy samples were collected during colonoscopy from the patients with colorectal polyps and ten healthy subjects for normalization. A questionnaire including clinical and demographic data was filled out for all cases. Mucosal mRNA expression of CD86 gene was investigated using Real-Time PCR and Fold Change of gene expression ($2^{-\Delta\Delta C_t}$) method.

Results: A total of 49 patients including 27(55.2%) male and 22(44.8%) female with mean age of 53 ± 15.3 were evaluated in this study. Adenoma and hyperplastic polyps were reported in 69.3% and 30.7% patients respectively. More than 90% of adenomatous polyps were spread out to the colon while the others were located in the rectum. Based on Relative Quantitation method, over-expression of CD86 genes in colon polyps were observed (Polyp ≥ 2 -fold normal) and down-expression of CD86 in rectum polyps were noticed in comparison with normal samples (Polyp ≤ 0.5 -fold normal).

Conclusion: Comparing mRNA expression level of CD86 gene in colon polyps with the profile of mRNA expression of polyps in the rectum indicates the presence of distinct molecular and immunological mRNA expression between polyps of these two sites.

Keywords: Colorectal Neoplasm, Colonic Polyp, Gene Expression, Antigens CD86

* Corresponding author. Tel: +98 21 22432525

hamid.assadzadeh@gmail.com

The attention needed for balance controlling in young patients with flatfoot

Rozita Hedayati (Ph.D)*, Elham Fatemi (MSc), Abdolhamid Hajihasani (Ph.D), Fateme Ehsani (Ph.D), Solaleh Ramezanzpour (MSc)

Neuromuscular Rehabilitation Research Center, Semnan University of Medical Sciences, Semnan, Iran

(Received: 3 Nov 2015; Accepted: 2 Aug 2016)

Introduction: Regarding to the importance of foot in maintenance of balance, it seems that flat foot can affect complex postural and balance control. In this study dual-task paradigm has been used to investigate the amount of attention needed for balance controlling in patients with flat foot than subjects with normal foot arch.

Materials and Methods: 30 participants (15 male & 15 female, mean ages $22/30 \pm 2/61$ years) with flat foot and 30 participants (15 male & 15 female, mean ages 22.30 ± 1.70 years) with normal foot arch were placed in two groups. Static & Dynamic balance tests were performed by Biodex Balance System SD under condition of single leg stance, in two forms of open and closed eyes. Measured parameters were total, anterior-posterior and medial-lateral stability indices.

Results: The within group comparison of single and dual tasks in control and flatfoot groups in static (open & closed eyes) and dynamic (open eyes) balance tests did not show any significant differences ($P > 0.05$). The within group comparison of single and dual tasks in two groups in dynamic balance condition with closed eyes showed significant differences ($P < 0.05$). The between group comparison of control and flatfoot groups in single and dual tasks in static (open & closed eyes) and dynamic (open and closed eyes) balance tests did not show any significant differences ($P < 0.05$).

Conclusion: The participants with flat foot have equal attentional demands in balance control compared to participants with normal foot arch.

Keywords: Attention, Postural Balance, Flatfoot

* Corresponding author. Tel: +98 9126090589

Rosehed@yahoo.com

Protein-protein interaction network analysis of human fibroblast cells treated with ethanol

Mona Zamanian-Azodi (Ph.D Student)¹, Mostafa Rezaei-Tavirani (Ph.D)*², Maryam Peyvandi (MD)², Akram Safaei (Ph.D Student)¹, Majid Rezaei-Tavirani (M.D)³, Mohammad Mahboubi (Ph.D)⁴, Farshad Okhovatian (Ph.D)⁵, Hossein Ali Safakhah (M.Sc)⁶

1 - Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2 - Proteomics Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3 - Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran

4 - Abadan School of Medical Sciences, Abadan, Iran

5 - Physiotherapy Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

6 - Physiology Research Center and Dept. of Physiology, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran

(Received: 15 Nov 2015; Accepted: 28 May 2016)

Introduction: Studies show that ethanol can induce changes in proteomic profile of human fibroblast cells. Some of these proteins are important in promoting cancer. Thus, analyzing function and interaction networks of these proteins are essential for better understanding the carcinogenesis mechanism of ethanol.

Materials and Methods: In this study the protein-protein interaction network (PPI) of six significant down-regulated proteins in human fibroblast cells (HFFF2) treated with ethanol were analyzed by using Cytoscape software and its algorithms.

Results: PPI network analysis showed that the constructed network consisted of 756 nodes and 1166 edges. Results indicated that Heterogeneous nuclear ribonucleoprotein A1 with degree = 528 and Betweenness Centrality = 0.74 is a hub protein that ethanol can alter its expression. In addition, module evaluation showed that the hub protein has a key role in different overlapped complexes. On the other hand, annotation studies by using DAVID program indicated that this protein is involved in different important biological processes in the cell.

Conclusion: The six down-regulated proteins treated with ethanol may become carcinogenic and can impose vast alterations in other vital biological processes of the cell. Among them, Heterogeneous nuclear ribonucleoprotein A1 is the most important one.

Keywords: Ethanol, Fibroblasts, Protein Interaction Maps, Gene Ontology

* Corresponding author. Tel: +98 98 21 22714248
tavirany@yahoo.com

The relationship between sleep quality in patients' undergoing hemodialysis at different therapeutic' shifts

Zaynab Hydarinia Naieni (M.Sc)¹, Monir Nobahar (Ph.D)^{2*}, Raheb Ghorbani (Ph.D)³

1 - Student Research Committee, Faculty of Nursing and allied health, Semnan University of Medical Sciences, Semnan, Iran

2- Nursing Care Research Center and, Faculty of Nursing and allied health, Semnan University of Medical Sciences, Semnan, Iran

3- Social Determinants of Health Research Center, Department of Community Medicine, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran

(Received: 21 Nov 2015; Accepted: 5 Jun 2016)

Introduction: Many hemodialysis patients suffer from poor sleep quality. The aim of this study was to determine the relationship between therapeutic' hemodialysis shifts with sleep quality in patients' undergoing hemodialysis.

Materials and Methods: This was a descriptive, cross-sectional study and participants were selected by available method, including 90 hemodialysis patients in Semnan who were undergoing hemodialysis in fixed morning, evening or night shifts for at least 3 months. Inclusion criteria included age over 18 years and hemodialysis 2-3 times per week for 3 hours or more per session. Sleep quality was assessed by Pittsburgh Sleep Quality Index (PSQI).

Results: In this study 54.4% of participants were male and the rest were female. Patients (33.3%) had good sleep quality and 66.7% had low sleep quality. Variable analysis showed a significant correlation between quality of sleep and sex ($P = 0.01$), marital status ($P = 0.009$), number of children ($P=0.012$) and dialysis' shift ($P = 0.003$). The effect of simultaneously variables in the logistic regression showed that the risk of low sleep quality in women versus men was 3.75/1, evening' versus morning shifts was 5.25/1 and night' versus morning shift was 4.13/1. Also, for each additional offspring, the risk of low sleep quality was increased to 1.33/1.

Conclusion: Findings in this study showed that sleep quality in patients that are hemodialyzed in morning shift was significantly better than the other shifts. These findings may help for arranging the situation to choose the most appropriate therapeutic shift for hemodialysis patients, especially for those who suffer from poor quality sleep.

Keywords: Hemodialysis, Sleep, Shift

* Corresponding author. Tel: ++98 023-33654170
nobahar43@Semums.ac.ir

Vulnerability factors of generalized anxiety disorder based on triple vulnerability model

Hamid Poursharifi (Ph.D), Jalil Babapour (Ph.D), HosseinKarsazi (M.Sc)*
Dept. of Psychology, University of Tabriz, Tabriz, Iran

(Received: 1 Dec 2015; Accepted: 15 May 2016)

Introduction: Triple vulnerability model focuses on the interaction of three types of vulnerabilities in development and maintenance of emotional disorders. Despite the prominence of this model, there is not enough research done to assess its experimental validity. The aim of this study was to evaluate vulnerability factors of generalized anxiety disorder based on triple vulnerability model.

Materials and Methods: For this purpose, 320 students from Tabriz University (Iran) were selected by cluster sampling and responses to NEO Five-Factor Inventory, Anxiety Control Questionnaire-revised, Intolerance of Uncertainty Scale and Generalized Anxiety Disorders Questionnaire-IV. Analysis was performed using structural equation modeling.

Results: Evaluation of hypothetical model using fit indices showed that the hypothetical model fitted with the measurement model. The results showed that neuroticism and extroversion have significant effect on generalized anxiety disorder by mediation of lack of perceived control and intolerance of uncertainty. In addition, hypothetical model was a better fit in compare to the alternative models.

Conclusion: our result, along with the support of triple vulnerability model for generalized anxiety disorder, proposes a suitable framework for the etiology of this disorder.

Keywords: Vulnerability factors, Generalized Anxiety Disorder, Triple Vulnerability Model

* Corresponding author. Tel: ++98 9141702327
hosseinkarsazi@gmail.com

Endometrial stem cells differentiation into neural cells by LY294002 small molecule

Homa Mohseni Kouchesfehaneh (Ph.D)^{*1}, Somaye Ebrahimi-Barough (Ph.D)², Jafar Ai (Ph.D)², Hamideh Anbar (M.Sc)³

1- Dept. of Animal Biology, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran

2 – Dept. of Tissue Engineering and Applied Cell Sciences, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

3 – Dept. of Animal Biology, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran

(Received: 3 Dec 2015; Accepted: 15 May 2016)

Introduction: Endometrial stem cells (EnSCs) were identified for the first time in 2004. These cells are capable of extensive self-renewal and have the potency to differentiate into chondrocyte, osteocyte, adipocyte, neuron and oligodendrocyte. PI3K/Akt signaling has been implicated in multiple cellular and organ functions, including differentiation, survival and cell death and its inhibition leads to cell differentiation. The purpose of this study was to investigate the differentiation of endometrial stem cells into neural cells by inhibition of PI3K/Akt pathway using small molecule Ly294002.

Materials and Methods: Endometrial tissues were treated enzymatically and segregated cells were cultured in DMEM/F12 with 10% FBS. The flow cytometry analysis was performed for CD105, CD90, CD146, CD31 and CD34 at the third passage. Then the neurogenic differentiation was evaluated at the third passage, 21 days after induction with differentiation media. Immunocytochemistry and Real-time PCR were performed to investigate the expression of specific neural stem cells markers.

Results: The flow cytometry analysis showed that EnSCs were positive for CD90, CD105 and CD146 and negative for CD31 and CD34. Immunocytochemistry showed that the expression of nestin, NF and Chat neuronal markers in the cells treated with small molecule Ly294002. Real-time PCR also indicated expression of NF and Chat neuronal markers at the mRNA level.

Conclusion: According to the findings of this study it can be concluded that the EnSCs have neural differentiation potency in the suitable differentiation milieu. Ly294002 small molecules by inhibiting PI3K / Akt pathway possibly can prevent cell proliferation and induce cell differentiation.

Keywords: Endometrium, Cell Differentiation, Stem Cells, Neural Cells, Phosphatidylinositol 3-Kinases

* Corresponding author. Tel: ++98 9123844874
kouchesfehaneh@yahoo.com

Designing a rapid and accurate method for transportation and culture of the *Campylobacter jejuni* and *Campylobacter coli*-fastidious bacteria in the children with bacterial gastrointestinal symptoms

Saeed Shams (Ph.D student)¹, Bakhshi Bita (Ph.D)^{*1}, Bahram Nikmanesh (Ph.D)^{2,3}

1 – Dept. of Medical Bacteriology, Faculty of Medical Sciences, TarbiatModares University, Tehran, Iran

2 - Zoonosis Research Center, Tehran University of Medical Sciences, Tehran, Iran

3 – Dept. of Medical Laboratory Sciences, School of Allied Medical Sciences, Tehran University of Medical Sciences, Tehran, Iran

(Received: 3 Dec 2015; Accepted: 30 Apr 2016)

Introduction: *Campylobacter* spp. is the major cause of bacterial gastroenteritis, called campylobacteriosis, in the worldwide. Post-infectious complications of this infection are reactive arthritis and Guillain–Barré syndrome. Despite the importance of this infection, the isolation of fastidiousbacteria cannot be performed in most clinical laboratories. The aim this study was to design an alternative transport medium with mCCDA and evaluation the bacteria survival time into this medium, optimization of culture conditions of bacteria and then performance of direct duplex-PCR on colonies and stool samples. Finally, the results of the PCR and culture were compared.

Materials and Methods: Fifty eight children suspected to campylobacteriosis were enrolled in this study. Fecal specimens were inoculated in depth inside the altered transport medium with mCCDA and then sent to laboratory. The specimens from transport media were cultured on two media of mCCDA&brucella agar daily and up to 7 days. Each plate was evaluated for bacterial growth up to 72 hours. The duplex-PCR on colonies and stool were carried out directly.

Results: Total of isolated bacteria in this study was 9 cases (16%). The colonies were visible on the media after 48 to 72 h. The duplex-PCR assay on colonies detected 8 isolates of *C. jejuni* and 1 isolate *C. coli*. The results of the direct duplex-PCR on fecal specimens and cultures were the same.

Conclusion: The results indicate that the presented method in this study with sensitivity equal to the PCR is useful for isolation of *Campylobacter* spp. It seems that using the changed transport medium and optimization of bacterial culture conditions will be isolated these fastidiousbacteria better than basic transport media.

Keywords: *Campylobacter jejuni*, *Campylobacter coli*, Cary-Blair, Duplex-PCR, Gastroenteritis

* Corresponding author. Tel: ++98 21 82884558

b.bakhshi@modares.ac.ir

Prevalence of *Toxoplasma gondii* and the level of IL8 in patients with Celiac disease

Mohammad Rostami-Nejad (Ph.D)^{1,2}, Seyed Hossein Hejazi(Ph.D)², Mehran Bahadoran(Ph.D)², Nader Pestehhian (Ph.D)², Mohammad Amin Pourhoseingholi(Ph.D)¹, Ahmad Hosseini-Safa(Ph.D)², Amir Sadeghi(M.D)¹, Hossein Nobakht (M.D)³, Reza Tajabadi Farahani (M.D)⁴, Mohammad Reza Zali(MD)¹

1- Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2 - Skin Disease and Leishmaniasis Research Center, Department of Parasitology and Mycology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

3 – Dept. of Internal Medicine, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran

4 - Shahid Beheshti University of Medical Sciences, Tehran, Iran

(Received: 26 Nov 2015; Accepted: 30 Apr 2016)

Introduction: *Toxoplasma gondii* infection is usually detected by using immunoglobulin IgG and IgM antibodies in different populations. This parasite is implicated in the pathogenesis of many autoimmune diseases such as celiac disease (CD). In the present study the prevalence of Toxoplasmosis and the level of IL8 in patients with Celiac disease were evaluated.

Materials and Methods: In this case-control study in 2013, 150 patients with CD diagnosis were selected by using questionnaire and the presence of antibodies specific for *Toxoplasma gondii* (IgG, IgM) was detected by ELISA. On the other hand the level of IL8 was detected using available commercial kit.

Results: patients (n=59, 39.9%) were positive for anti-toxoplasma IgG. On the other hand, only 2 of them were positive for IgM antibodies, which did not show statistical correlation to the disease (1.4%, P = 0.65). The mean level of IL8 was 176.38 (SD=191.79) in 150 CD patients, which did not show a statistical significant correlation between the mean level of IL8 and celiac disease (P=0.001).

Conclusion: Like other studies showing that intestinal infection can help to develop celiac disease in susceptible individuals, our results also revealed that *Toxoplasma gondii* infection can increase the risk of developing celiac disease.

Keywords: Coeliac Disease, Toxoplasmosis, Serology, Interleukin-8

* Corresponding author. Tel: ++98 9133118711

hejazi@med.mui.ac.ir

Topological analysis of blood differentially expressed genes in protein-protein interaction network in type 1 diabetes

Nahid Safari-Alighiarloo (Ph.D student)¹, Mohammad Taghizadeh (Ph.D student)², Seyyed Mohammad Tabatabaei (Ph.D student)³, Soodeh Shahsavari (Ph.D student)⁴, Saeed Namaki (Ph.D)⁵, Soheila Khodakarim (Ph.D)⁶, Mostafa Rezaei-Tavirani (Ph.D)^{*1}, Ali Rashidy-pour (Ph.D)⁷

1-Proteomics Research Center, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2- Bioinformatics Dept., Institute of Biochemistry and Biophysics, Tehran University, Tehran, Iran

3- Medical Informatics Department, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

4- Biostatistics Department, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

5- Dept. of Immunology, Faculty of Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

6-Department of Epidemiology, School Of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran

7- Physiology Research Center and Dept. of Physiology, Faculty of Medicin, Semnan University of Medical Sciences, Semnan, Iran

(Received: 4 Dec 2015; Accepted: 21 May 2016)

Introduction: Type 1 diabetes (T1D) results from autoimmune destruction of insulin-producing beta cells in pancreatic islets of Langerhans. To develop efficient treatments for T1D, it is required to identify suitable therapeutic markers. Systems biology offers approaches to better understanding of functional elements in the disease. Our aim was to investigate larger number of candidate markers in T1D by topological analysis of constructed PPI based on gene expression.

Materials and Methods: In this study, gene expression profile of peripheral blood mononuclear cells from newly diagnosed type 1 diabetic children was prepared from Gene Expression Omnibus and analyzed to get differentially expressed genes. Then, these genes were mapped to PPIs data to construct related subnetwork. Five topological features were calculated by Cytoscape software. Finally, degree, betweenness and closeness centrality features were utilized to identify candidate markers.

Results: 2467 differentially expression genes were obtained by statistical analyzing of gene expression profile in which 1024 were upregulated and 1443 were downregulated. After mapping these genes on PPI network, there was constructed subnetwork with 949 nodes and 1776 edges. By topological analysis of the subnetwork, we determined high degree nodes (hub) and high betweenness nodes (bottleneck). Then, 9 hub-bottleneck proteins that were more central (high closeness centrality) in the subnetwork were identified and introduced as candidate markers.

Conclusion: The obtained markers from network via systemic view can be considered as new diagnostic markers and potential therapeutic targets for T1D.

Keywords: Type 1 Diabetes, Gene Expression, Protein-Protein Interaction Network

* Corresponding author. Tel: ++98 21 22714248

tavirany@yahoo.com

Application of log-normal parametric model in disability structure to predict metastasis and death due to breast cancer

Morteza Hajihosseini (M.Sc)¹, PayamAmini (Ph.D Student)², Maryam Shahdoust (Ph.D Student)³, Javad Faradmal (Ph.D)^{*4}, Majid Sadeghifar (Ph.D)⁵, Abdolazim Sedighy-Pashaki (M.D)⁶

1- Dept. of Biostatistics & Epidemiology and Students Research Center, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran

2 - Dept. of Epidemiology and Reproductive Health, Reproductive Epidemiology Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran

3 - Modeling of Noncommunicable Diseases Research Center & Department of Biostatistics, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran

4 - Modeling of Noncommunicable Diseases Research Center, Dept. of Biostatistics and Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran.

5 - Dept. of statistics, School of Basic Sciences Bu-Ali Sina University, Hamedan, Iran

6 - Radiology-Oncology Center, MRI Center of Hamadan Darol-Aitam, Hamadan, Iran

(Received: 6 Dec 2015; Accepted: 15 May 2016)

Introduction: Determining disease progression process and its affecting factors are of the most important issues in controlling the disease. This study aimed to predict the breast cancer progression as well as assessing the relationship between demographical and clinical factors.

Materials and Methods: This retrospective cohort study was conducted on 527 Iranian females with breast cancer who underwent surgery, from 1995 to 2013 using checklists. The effect of the factors on death and tumor recurrence was assessed by log-normal model fitted into each transition of illness-death model which were used to investigate the relationship between demographic and clinical factors and survival time. Data analysis was performed using statistical R software version 3.1.1. The significance level of 0.05 was considered.

Results: Evaluating the hazard of death without recurrence, the risk of death in patients over 50 years were higher than those under 50 ($P=0.01$). A tumor size of 2-5 cm was introduced as a death factor in recurrent patients ($P=0.01$). Age and type of tumor did not impact the hazard. Log-normal distribution was chosen for downtime between steps.

Conclusion: Based on the results, age at diagnosis had significant impact on the risk of death before the first recurrence. Tumor size had a significant effect on death after tumor recurrence. In addition, Log-normal and disability models are appropriate tools to identify the factors influencing survival of patients with breast cancer.

Keywords: Survival Analysis, Breast Neoplasms, Neoplasm Metastasis, Statistical Models, Disability Structure

* Corresponding author. Tel: ++98 9124055256

javad.faradmal@umsha.ac.ir

Relationship between the forward head and thoracic hyperkyphosis deformities with body image in non-athletes females

Foad Seidi (Ph.D)*, Leila Sadat Ghasabi (M.Sc), Elahe Fadaee (M.Sc)
Dept. of Health and Sport Medicine, Faculty of Physical Education and Sport Sciences, University of Tehran, Tehran, Iran

(Received: 14 Dec 2015; Accepted: 5 Jun 2016)

Introduction: The state of health and illness in each of physical or mental dimensions can influence on the other dimension. Thus, it is essential to study interaction between physical deformities and mental variations. Nevertheless, this issue already is not considered sufficiently. The objective of present research was to study the relationship between deformities of the spine including forward head and thoracic hyperkyphosis with body image in non-athletes females.

Materials and Methods: One hundred twenty non-athletes female who their ages ranged from 25 to 30 years old, were participated in this study. These participants were divided into two groups, with each group had 60 members and were associated with one of the deformities including forward head and thoracic kyphosis. The angle of thoracic kyphosis was measured by flexible ruler and forward head was measured by photogrammetry method.

Results: Data in both descriptive and inferential statistics were analyzed using SPSS version 19. The relationship between the spine deformities was assessed by Pearson correlation coefficient. Results show that although there was a significant relationship between body image and kyphosis abnormality in non-athlete girl student ($r = 0.951$, $p = 0.008$) but there was also no significant relationship between body image and forward head ($r = 0.29$, $p = 0.21$).

Conclusion: It seems that in deformities such as thoracic kyphosis that is physically evident and is well known by most people; body image weakness is more. So, lack of awareness about forward head posture may decrease the person's sensitivity to their appearance. Although psychological, economical, business, lifestyle and cultural as well as factors other relevant factors most be considered.

Keywords: Body image, Forward head, Hyper-kyphosis, Postural deformities, Photogrammetry

* Corresponding author. Tel: ++98 9126781740
foadseidi@ut.ac.ir

Expression and characterization of recombinant human epidermal growth factor receptor antigene (HER-2) as an indicator of breast cancer in yeast fermented systems

Saeideh Foroumadi (M.Sc)¹, Masoumeh Rajabibazl (Ph.D)^{*1}, Seyed Hossein Hosseini (M.Sc)¹, Shirin Rajabi (M.A.)², Solmaz Shahidi (M.Sc)¹, Azam Daraei (B.Sc)¹, Attabak Toofani Milani (M.Sc)¹

1 - Dept of Clinical Biochemistry, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2 - University of Tehran

(Received: 21 Dec 2015; Accepted: 27 Aug 2016)

Introduction: Immunotherapy has been practiced for more than two decades in the treatment of cancer. In this method, monoclonal antibodies bind to tumor specific antigens and inhibit their function. Therefore, scientists are looking for special targets on cancer cells that can be differentiate cancer cells from normal cells. In some cancers, including breast cancer human epidermal growth factor receptor-2 (HER-2) is significantly higher than the normal level. The goal for this project was to obtain expression with high quality of HER-2 with high activity in yeast expression system and its use in future studies.

Materials and Methods: In order to express the extracellular domain of the HER-2 receptor we have used pPICZα and *Pichia pastoris wild type X33* as a sequence vector and host cell respectively. Expression of HER-2 was analyzed using Sodium Dodecyl Sulfate Poly Acrylamide Gel Electrophoresis 7% and accuracy of expression was confirmed by ELISA.

Results: The expression of Her-2 antigen was evaluated by 7% SDS-PAGE with 185 KDa protein ladder. The results indicated that the expression of Her-2 antigen has been increased by IPTG induction. Moreover, the activity of Her-2 antigen was studied by ELISA technique using commercial anti Her-2 monoclonal antibody (Herceptin) and Her-2 antigen has shown high affinity to Herceptin.

Conclusion: In this study, we have produced the Her-2 antigen in yeast expression system. With regards to yeast expression system advantages including secretory expression, protein folding, protein glycosylation, and activity of expressed protein in a wide range of pH, the Her-2 antigen which expressed in yeast host has great quality and will be used in future studies

Keywords: Brest Cancer, HER-2, *Pichia pastoris*

* Corresponding author. Tel: ++98 21 23872570

rajabi_m@sbmu.ac.ir

Effects of addition of different probiotic strains on the biochemical and microbiological properties of Aloe vera drink

Zahra Sarlak (M.Sc)¹, Reza Mohammadi (Ph.D)², Khadije Abdolmaleki (Ph.D)³, Amir Mohammad Mortazavian (Ph.D)^{*4}, Mahdi Shadnoosh (Ph.D)^{6,5}

1- Dept. of Food Hygiene and Quality Control, School of Nutrition and Food Sciences, Nutrition and Food Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

2- Dept. of Food Science and Technology, Faculty of Public Health, Kermanshah University of Medical Sciences, Kermanshah, Iran.

3- Students' Research Committee, National Nutrition and Food Technology Research Institute, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

4. Dept. of Food Science and Technology, Faculty of Nutrition Sciences and Food Science and Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

5 - Dept. of Nutrition, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran

6 – Dept. of Clinical Nutrition, Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

(Received: 30 Dec 2015; Accepted 8 Jun 2016:)

Introduction: Recently, an increased demand for nondairy probiotic products comes from the vegetarians, those with lactose intolerance and high cholesterol blood content in dairy products. In this research, the effects of adding different probiotic strains to the Aloe vera drink were studied on biochemical and microbiological specifics during refrigerated storage.

Materials and Methods: About 7% of any cultured single strain probiotic (*Lactobacillus* (*L.*) *acidophilus*, *Lactobacillus casei*, *Lactobacillus reuteri*, *Lactobacillus fermentum* *Lactobacillus plantarum*) were added to Aloe vera juices. Samples were studied in 7 days intervals throughout 21 days of storage at 5°C. pH and redox potential values were measured by pH-meter. Titrable acidity value was determined by titration with 0.1 N NaOH. Probiotic bacteria were enumerated using MRS-agar medium.

Results: The highest and lowest biochemical changes were observed in treatments with *L. reuteri* and *L. acidophilus*, respectively. Therefore, different types of inoculated probiotic strains, with different ability in fermentation at refrigerated temperature, had effects on the amount of the biochemical changes during storage. The most probiotic viable counts in treatments with *L. acidophilus* were observed at the end of storage.

Conclusion: Probiotic viability was improved in Aloe vera juices probably due to high amounts of nutrients such as aminoacids, proteins, sugars, vitamins, phenolic compounds and antioxidants. *L. acidophilus* and *L. fermentum* are suitable choice to use in Aloe vera drink.

Keywords: Aloe vera, Beverages, Probiotic

* Corresponding author. Tel: ++98 21 22376426

mortazvn@sbmu.ac.ir

Captopril inhibited metamphetamine - induced cardiac mitochondrial damage in hyperthermic condition via modulation of biochemical markers

Mohammd Shokrzadeh (Ph.D)^{1,2}, Ehsan Zamani (Pharm.D)^{1,2}, Javad Mollahasani (Pharm.D)^{1,2}, Fatemeh Shaki (Ph.D)^{*1,2}

1 - Pharmaceutical Sciences Research Center, Mazandaran University of Medical Sciences, Sari, Iran

2 - Dept. of Toxicology and Pharmacology, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

(Received: 5 Jan 2016; Accepted: 30 Apr 2016)

Introduction: Methamphetamine (METH) is a known abused drug which could induce cardiotoxicity. Captopril is an angiotensin converting enzyme inhibitor that is used in hypertension therapy and has known antioxidant effects. In this study we evaluated the effect of captopril against METH-induced toxicity in rat heart isolated mitochondria in hyperthermic condition.

Materials and Methods: Mitochondrial fractions were isolated from heart of Wistar rat with different centrifuge technique. Then, heart isolated mitochondrial were exposed to METH (LC50, 250 μ M) and captopril (0, 25, 50, 100, 200, 400 μ M) and incubated at 37 and 41 C. After 1 h incubation, mitochondrial damage was assayed by MTT test. Also, oxidative stress markers were measured.

Results: Our results showed that METH significantly induced mitochondrial damage that was more pronounced in hyperthermic condition. Increased oxidative stress markers such as lipid peroxidation, reactive oxygen species formation and glutathione oxidation in the heart isolated mitochondria were observed after METH exposure that was more significant at 41 c than 37 C. Captopril significantly inhibited METH-induced oxidative stress in the heart isolated mitochondria. Also, captopril pretreatment significantly improved mitochondrial function. Mitochondrial swelling also increased after METH exposure, but was significantly decreased with captopril pre-treatment.

Conclusion: These results suggested that captopril could ameliorate METH-induced oxidative stress and mitochondrial dysfunction especially in hyperthermic condition. Therefore, the effectiveness of this antioxidant should be evaluated for the treatment of METH cardiotoxicity.

Keywords: Captopril, Methamphetamine, Cardiotoxicity, Mitochondria; Oxidative Stress, Rat

* Corresponding author. Tel: +98 9112559051

fshaki.tox@gmail.com

Effects of increasing walking speed on ankle muscle co-contraction based on spasticity severity in chronic stroke patients

Roghayeh Mohammadi (Ph.D)^{*1}, Solmaz Mohammadzadeh Nanehkaran (M.Sc)²

1 - Neuromuscular Rehabilitation Research Center and Rehabilitation Faculty, Semnan University of Medical Sciences, Semnan, Iran

2 - Occupational Therapist in Welfare Organization, Ardabil, Iran

(Received: 16 Jan 2016; Accepted: 5 Jul 2016)

Introduction: Plantar flexor muscles produce propulsive force in the second half of stance phase; deficient motor output from these muscles would lead to inadequate propulsion at push off phase of gait following stroke. The aim of the present study was to examine the effects of walking on a treadmill at varying speeds on ankle muscle activation in stroke survivors and to compare the effect of increasing speed on plantar flexor muscle activity in subject groups in relation to spasticity severity.

Materials and Methods: Nineteen stroke survivors (13M/6F) walked on a standard treadmill at three different speeds (self-selected, self-selected+20%, self-selected+40%). The electromyographic activity of *Medial Gastrocnemius (MG)*, and *Tibialis anterior (TA)* muscles recorded at push off phase of the gait.

Results: In the high spasticity subgroup (Tardieu scale ≥ 2), paretic MG activity increased as walking speed increased ($p < 0/05$).

Conclusion: Our data indicates that individuals with stroke can be safely trained on a treadmill to walk 20-40% above the self-selected pace to improve MG output without adversely affecting TA output.

Keywords: walking; Electromyographict Stroke

* Corresponding author. Tel: ++98 9143570295
mohamadpt@gmail.com

Levels of plasma immunoglobulin E in patients with chronic lymphocytic leukemia and breast cancer

Mehrnoosh Pashaei (M.Sc)^{1,2}, Mehdi Barati (M.Sc.)^{†1}, Ehsan Manouchehri Doulabi (M.Sc)^{1,5}, Farahnaz Ghahremanfard (M.D)³, Majid Mirmohammadkhani (M.D)⁴, Fatemeh Pak (Ph.D)¹, Parviz Kokhaei (Ph.D)^{*1, 5}

1- Cancer Research Center and Department of Immunology, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran

2- Student Research Committee, Semnan University of Medical Sciences, Semnan, Iran

3- Internal Medicine Department, Semnan University of Medical Sciences, Semnan, Iran

4- Social Determinants of Health Research Center, Department of Community Medicine, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran

5- Immune and Gene Therapy Lab, Cancer Centre Karolinska, Karolinska University Hospital, Stockholm, Sweden

(Received: 30 Jan 2016; Accepted: 11 Sep 2016)

Introduction: Immunoglobulin E (IgE) is a key player in allergy diseases and immune responses against parasites. Epidemiological studies indicated that there is an inverse association between plasma IgE levels as it been seen in allergic patients and the risk of cancer development. The aim of this study was to investigate the plasma IgE levels in breast cancer and patients with chronic lymphocytic leukemia healthy subjects.

Materials and Methods: In this case-control study, twenty patients with CLL also twenty five patients with breast cancer as the cases groups and twenty age-matched healthy subjects as control group were evaluated. Plasma IgE levels in both groups were measured by ELISA. Data from both groups were analyzed and compared by kolmogorov-smirnov test and paired t-test with SPSS version 16.

Results: The IgE levels were 9.045 ± 4.261 IU/ml in CLL patients and 37.19 ± 12.21 IU/ml in patients with breast cancer and 40.73 ± 16.18 IU/ml in healthy subjects. Our data showed that plasma IgE levels in CLL group were significantly less than controls group ($p < 0.05$), however the difference between patients with breast cancer and controls group was not significant.

Conclusion: It seems that there is an inverse correlation between serum IgE levels and the risk of developing CLL. While there is no correlation between the IgE level and the risk of developing breast cancer. IgE levels might be used as a biological marker in chronic lymphocytic leukemia development.

Keywords: Breast Neoplasms, Chronic lymphocytic leukemia, Immunoglobulin E, Enzyme-Linked Immunosorbent Assay

* Corresponding author. Tel: +98 23 33654362

† Equal with first author

parviz.kokhaei@ki.se

Relationship between idiopathic hypercalciuria and urinary tract infection in children of 1-14 years of age

MohamadSadegh Yazdiha (M.D)¹, Raheb Ghorbani (Ph.D)², Javad Behshad (M.D)¹, Seyyed Mohamad Hoseini (MD)¹, Mohammadreza Razavi (MSc)^{*3}, AlirezaEmadi (B.Sc)⁴

1- Dept. of Pediatric, Semnan University of Medical Sciences, Semnan, Iran

2- Research Center of Physiology, and Social Determinants of Health Research Center, Department of Community Medicine, Semnan University of Medical Sciences, Semnan, Iran

3- Nursing Care Research Center, Student Research Committee, Semnan University of Medical Sciences, Semnan, Iran

4- Information Technology Unit, Deputy of Research and Technology, Semnan University of Medical Sciences, Semnan, Iran

(Received: 2 Feb 2016; Accepted: 1 Aug 2016)

Introduction: Urinary tract infection (UTI) is one of the most common causes of chronic renal failure of children. Therefore diagnosis of predisposing factors have an important role to prevent renal damage. This Study was performed to investigate the association between idiopathic hypercalciuria and urinary tract infection in children 1-14 years of age admitted to Amiralmomenin hospital of Semnan (Iran).

Materials and Methods: This was a case-control study in which 75 children with UTI (without renal stone and urinary tract malformation) and a control group of 75 children without UTI were investigated. We measured random urine calcium to creatinine ratio in these children. In order to ruled out of secondary hypercalciuria, serum calcium, phosphor alkalene phosphatase, venous blood gases also were measured.

Results: 67 out of 150 patients (89.3%) were females and the rest were males. The mean (\pm SD) age of children with UTI were 3.83 ± 2.78 years and in control group were 3.88 ± 2.88 years which the difference was not significant ($p = 0.907$). Idiopathic hypercalciuria in 40% ($n = 30$) of children with UTI and 13.3% ($n = 10$) of children without UTI was found ($P < 0.001$, CI: 1.81-10.60, OR = 4.33). The number of male children affected by UTI with hypercalciuria were significantly more than girls with UTI and hypercalciuria ($p < 0.001$).

Conclusion: Based on results of this study, idiopathic hypercalciuria has a significant correlation with UTI in children and investigation of urinary calcium excretion in children with UTI is recommended.

Keywords: Urinary Tract Infection, Hypercalciuria, Preschool Child

* Corresponding author. Tel: ++98 23 33448950
mrrazavi@yahoo.com

Evaluation of time-stability response of gelatin-Trimesic acid dosimeter

Ramzan Ali Ramzanpour (M.Sc)¹, Zohreh Hoseinpour Yektaei (M.Sc)², Maryam Rahbar (M.D)^{3,4}, Hadi Hasanzadeh (Ph.D)^{*1,4}

1 – Student Research Committee, Dept. of Medical Physics, Semnan University of Medical Sciences, Semnan, Iran

2- Dept. of Radiotherapy, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

3 - Deputy of Research, Semnan University of Medical Sciences, Semnan, Iran

4 - Cancer Research Center, Semnan University of Medical Sciences, Semnan, Iran

(Received: 7 Feb 2016; Accepted: 2 Aug 2016)

Introduction: One of the problems in chemical dosimeters such as Trimesic acid is the liquid environment which makes it difficult to use. Chemical dosimeter merged into a bed of gel can help to partly overcome this problem. According to the importance of stability of dosimeter response after irradiation, in this study, the parameters of gelatin- Trimesic acid dosimeter in the range of doses of a one fraction of radiotherapy was assessed in days one, two, three and four after irradiation.

Materials and Methods: After the gel construction at a concentration of 1 mM and a pH of 2.2, it was poured into Perspex vials which opening was tight with parafilm and wrapped in an aluminum foil to eliminate light and was divided into 5 groups to be irradiated with 6 MV photons of linac 24h after the gel synthesis. To do so, vials were placed at the isocenter of the linac in a SSD of 100cm and field size of 10×10 cm². The delivered doses were from 0-200 cGy and vials were kept at the temperature of 4°C after the irradiation. The procedure of reading the vials were performed using a spectrofluorimeter (Jasco 6200) from one to four days after irradiation in excitation wavelengths of 370, 380, 390, 410, 420 and 450 nm.

Results: After obtaining the emission spectrum from the spectrofluorimeter, the emission spectrum was analyzed and it was found that there is a peak in the wavelengths of 377, 387, 396, 416, 427 and 457 nm seen in one day after irradiation and the most stable response belongs to the first day after irradiation.

Conclusion: The results of this study showed that the combined gelatin- Trimesic acid dosimeter in the first day after irradiation has the highest and most stable response and according to its characteristics, has the potential to be assessed as a clinical dosimeter.

Keywords: Chemical dosimetry, Gelatin- Trimesic acid, Stability, Spectrofluorimetry

* Corresponding author. Tel: +98 23 33451337

Hasanzadeh.h@semums.ac.ir

Effects of dietary conjugated linoleic acid on serum visfatin level and tumor number and size in rat model of colorectal cancer

Zahra kamal (M.Sc student)¹ Marjan Ajami (Ph.D)², Nasrin Beheshti (M.Sc student)¹, Morteza Abdollahi (Ph.D)², Sayed Hossein Davoodi (Ph.D)^{*3,4}

1- Dept. of Nutrition and Food Science, Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2 – Dept. of Food and Nutrition Policy and Planning Research, National Nutrition and Food Technology Research Institute, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3 - Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

4 - Dept. of Nutrition Research, National Nutrition and Food Technology Research Institute, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

(Received:; Accepted:)

Introduction: Colorectal cancer is the third causes of cancer death in the world. Recent studies have shown that the serum levels of visfatin are increased during malignancies, suggesting a role for visfatin in pathogenesis of malignancies. It is suggested that conjugated linoleic acid, (CLA) can reduce the serum levels of visfatin. The aim of this study was to study the effects of dietary conjugated linoleic acid on serum visfatin level in rat model of colorectal cancer.

Materials and Methods: Sixteen male Wistar rats, weighing 250-300 g were divided into two groups: control and experimental. Both groups were injected subcutaneously, with 1,2- Dimethyl Hydrazine at a dose of 15 mg/kg of body weight, twice per week for 6 weeks. The control group and experimental groups were gavaged with water (2 ml/kg) and CLA (200 mg/kg), respectively, for the first 4 weeks of study. After 6 weeks, the rats were killed and their blood and colorectal tissues were collected in order to analyze serum visfatin, tumor number and tumor size respectively by ELISA method, tumor numbering and macroscopic analysing.

Results: Visfatin levels decreased dramatically in the experimental group than control group ($P=0.001$). Tumor number and tumor size increased considerably in the control group than experimental group ($P = 0.000$). There was a positive correlation between visfatin levels with tumor number ($r =0.701$, $p = 0.001$) and also between plasma visfatin with tumor number×tumor size ($r=0.771$, $p=0.000$).

Conclusion: This study shows that dietary CLA by reducing serum visfatin can decrease the tumor number and tumor size in rat model of colorectal cancer. Thus, CLA suppresses colon carcinogenesis by a mechanism probably involving reduced serum visfatin.

Keywords: Visfatin, Conjugated linoleic Acid, Colorectal cancer

* Corresponding author. Tel: ++98 9128115284
hdavoodi1345@gmail.com

Prevalence *Atopobium vagina* in vaginal samples of symptomatic non-pregnant women

Hamideh Maftoon (M.Sc)¹, Nour Amirmozafari (Ph.D)^{*2}, Maryam Kashanian (M.D)³, Mojgan Oshaghi (Ph.D)⁴

1 - Microbiology Dept., School of Medicine, Iran University of Medical Sciences, Tehran, Iran

2 - Microbiology Dept., School of Medicine, Iran University of Medical Sciences, Tehran, Iran

3 - Obstetrics and Gynecology Dept., School of Medicine, Iran University of Medical Sciences, Tehran, Iran

4 - Laboratory Science Dept., School of Paramedicine, Iran University of Medical Sciences, Tehran, Iran

(Received: 20 Feb 2016; Accepted: 25 Jul 2016)

Introduction: Bacterial vaginosis is not a mono-factorial infection. A synergism of microaerophilic bacteria, *Mycoplasma* spp., and anaerobic bacteria such as *Atopobium vaginae*, *Porphyromonas* spp., *Bacteroides* spp., *Prevotella* spp., and others are involved in these infections. The aim of present study was to determine the prevalence of *Atopobium vaginae* in non-pregnant women suffering from bacterial vaginosis.

Materials and Methods: A total of 102 non-pregnant women who referred to ShahidAkbarabadi hospital in Tehran were tested for bacterial vaginosis. In order to isolate *Atopobiumvaginae* the sample was cultured on Colombia agar containing Amphotericin B, Nalidixic acid and Colistin. Additionally, they were simultaneously cultured on blood agar plates containing fresh human blood and Amphotericin B under anaerobic conditions. After extraction DNA from colonies and vaginal specimens, PCR amplification was performed by using specific primers for detection of *Atopobiumvaginae*.

Results: From a total of 102 women who referred to the hospital, 38 cases were confirmed for bacterial vaginosis. With PCR assay, 25 of these 38 cases (%65) were positive for *Atopobiumvaginae*.

Conclusion: This is the first report of isolation of *Atopobiumvaginae* in Iran. The results of this investigation points to a clear association of *Atopobiumvaginae* with bacterial vaginosis and *Atopobiumvaginae* should also be considered as a probable etiological agent.

Keywords: Bacterial Vaginosis, Female, Women, Polymerase Chain Reaction

* Corresponding author. Tel: +98 9123877988
amirmozafari@yahoo.com

Effects of margarine and butter on lipid profile and serum fatty acid composition in rats

Ali heshmati (Ph.D)^{*1}, Ali asghar vahidinia (Ph.D)²

1 – Nutrition Health Research Center, Hamadan University of Medical Sciences and Health Services, Hamadan, Iran

2 - Dept. of Nutrition, Medicine School, Hamadan University of Medical Sciences and Health Services, Hamadan, Iran

(Received: 25 Feb 2016; Accepted: 5 Jul 2016)

Introduction: Cardiovascular disease is the leading cause of death in the world. Nutritional factors are one of the main causes of these diseases. Food regimes that are rich in saturated and trans fatty acids increase the risk of these diseases. The aim of this study was to investigate the impact of hard and soft margarine, butter and canola oil (control group) on serum lipid profile of rats.

Materials and Methods: Thirty-two rats were divided into four groups for eight weeks with a high-fat diet containing canola oil, hard and soft margarine or animal butter. Fatty acid composition and lipid profile of serum were measured before and after the intervention.

Results: Compared to canola oil, margarine and animal butter led to a significant increase in triglyceride. In all groups, total cholesterol and HDL-C were increased. Canola oil reduced LDL-C and hard margarine, but not soft margarine and also butter increased it. Butter increased LDL-C/HDL-C but margarine and canola oil reduced it. In serum of the control group, the levels of saturated fatty acids reduced, but those of mono- and poly-unsaturated fatty acids increased. The reverse changes were found in the butter and margarine groups.

Conclusion: In compared with butter, high-trans margarines have a negative impact on lipid profile, while low-trans ones caused improvement lipid profile.

Keywords: Margarine, Butter, Cholesterol, Triglyceride, Lipid, Fatty Acid

* Corresponding author. Tel: +98 81 38381821

a.heshmati@umsha.ac.ir

Determination of validity and reliability of the Bayley scales in infant and toddler development

Nadia Azari (M.D)¹, Farin Soleimani (M.D)^{*1}, Roshanak Vameghi (M.D)¹, Firouzeh Sajedi (M.D)¹, Soheila Shahshahani (M.D)¹, Hossein Karimi (M.D)¹, Adis Kraskian (Ph.D)², Amin Shahrokhi (M.D)¹, Robab Teymouri (Ph.D)¹, Masoud Gharib (Ph.D Candidate)¹

1 - Pediatric Neurorehabilitation Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

2 – Dept. of counseling & guidance, Karaj Branch, Islamic Azad University (IAU), Karaj, Iran

3- Faculty of Paramedicine, Mazandaran University of Medical Sciences, Sari, Iran

(Received: 6 Mar 2016; Accepted: 27 Jul 2016)

Introduction: For diagnosing children who are suspected to have developmental delay through developmental screening tests, we need a valid and reliable diagnostic tool. The Bayley scales is a well-known diagnostic developmental assessment on cognitive, communication and motor domains. The aim of this study was validity and reliability determination of the Bayley test.

Materials and Methods: The method of this study was descriptive-analytic. The test was provided through translation- back translation and cultural adaptation. Content and face validity of tool was determined by experts' opinions. 260 children aged 1 to 42 months were recruited for developmental assessment by Bayley. Reliability of test was calculated through three methods; internal consistency, test-retest and inter-rater. Construct validity was calculated using factor analysis and comparison of the mean scores methods.

Results: Participants were 260 children 15 days to 42 months, including 134 boys (51.5%). Cronach's alpha coefficients were more than 0.76 for all domains. Pearson correlation coefficient in different domains, were at least 0.987 ($P < 0.001$) in test retest method; and 0.991 ($P < 0.001$) in inter-rater method. The face and content validity of test was approved by experts in child development. Construct validity of test was approved through factor analysis and statistically significant differences were observed between mean scores of different age groups, that confirms the validity of test.

Conclusion: These results indicated that the Bayley is a valid and reliable tool for developmental assessment in Persian children.

Keywords: Child Development, Infant, Reproducibility of Results, Neuropsychological Tests

* Corresponding author. Tel: +98 21 22180099

Soleimani_farin@yahoo.com

The importance of radiography after reduction of anterior shoulder dislocation

Farah Hashemi (M.D)¹, Davood Sharifi (M.D)¹, Majid Kasaei(M.D)^{1,3}, Elahe Ghasemi(M.D)¹, Mohammadreza Razavi (M.Sc)², Sabahat Lavvaf (M.D)³, Hamid Zamani-Moghadam (M.D)^{*1}

1 - Dept. of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

2 - Nursing Care Research Center, Student Research Committee, Semnan University of Medical Sciences, Semnan, Iran

3 - Semnan University of Medical Sciences, Semnan, Iran

(Received: 7 May 2016; Accepted: 11 Sep 2016)

Introduction: Dislocation of shoulder joint is the most common joint dislocation in the body. This dislocation is the most common one in the 2nd period of life. In men between 20-30 years of age due to trauma and sports activities and in women between 60-80 years, usually due to increases in fall. The aim of this study was to determine the prevalence of abnormal radiography in the reduction of anterior shoulder dislocation.

Materials and Methods: In a one-year cross sectional study, 236 patients with uncomplicated anterior shoulder dislocation who referred to Imam Reza hospital (Mashhad, Iran) were studied. The following data were obtained and recorded: the age and gender of patients, mechanism of injury, radiographs before replacing it up and the interpretation of results, the result of reduction and shoulders immediately following graph reduction, the result of the interpretation of radiographs after reduction, the dislocation and reduction.

Results: The mean age of patients was 31.81 ± 13.22 . 174 patients (89%) were male and 26 (11%) were female. Anterior dislocation in 116 patients (49.2%) were right shoulder and in 120 patients (50.8%) were left shoulder. Spontaneous dislocation (61.9%) was the most dislocation mechanism and the external rotation (46.4%) was the most reduction method. Physical examination before and after reduction, and the interpretation of radiographs after reduction indicated the correction of anterior shoulder dislocation in all patients.

Conclusion: This study demonstrated that radiography after anterior shoulder dislocation reduction is not necessary.

Keywords: Shoulder Dislocation, Radiography

* Corresponding author. Tel: +98 9127312407
are20935@yahoo.com

Effects of different doses of manganese on lead poisoning in the kidney of adult male mice

Shabnam Mohammadi (Ph.D)¹, Mahbobeh Khakbaz (M.D Student)^{*2}, Marzieh Shoraka (M.D Student)², Samira Vakil (M.D Student)², Maryam Moghimian (Ph.D)³, Fatemeh mohammadzadeh(M.Sc)³, Maryam Mohammadi (Ph.D)⁴, Naghmeh jajarmi (M.Sc)⁵, Kamyar Tavakkoli (MD)⁶, Mehdi Basiri Moghadam (M.Sc)⁷, Mehdi Karimi (MD)⁸

1- Neurogenic Inflammation Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

2 - Student Research Committee, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran

3 – Dept. of Basic Sciences, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran

4 - Dept. of Public Health, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

5 – Student of Biochemistry, PayameNoor University, Mashhad, Iran

6 - Dept. of Urology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

7 - Dept. of Nursing, Faculty of Nursing, Gonabad University of Medical Sciences, Gonabad, Iran

8 - Dept. of Clinical Sciences, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran

(Received: 17 Feb 2015; Accepted: 9 May 2016)

Introduction: Lead is one the heavy metals that cause negative effects on the body systems. However, there is little data about the effect of antioxidants on kidney damage induced by the lead. Therefore, the aim of the present study was to evaluate the effects of different doses of manganese on biochemical and histopathological parameters of kidney in mice.

Materials and Methods: In this study, 48 adult Balb/C male mice were randomly divided into six groups. Control group did not receive any injection. Second group received 60 mg/kg lead acetate intraperitoneally. Third to sixth groups were injected 60 mg/kg lead acetate and 2.5-5-10-20 mg/kg manganese intraperitoneally, respectively. After 14 days, slides from kidney of mice prepared and the volume of kidney and volume and number of glomeruli were measured by stereological method. Besides, levels of serum urea and creatine were measured.

Results: Evaluation of the kidney tissue in lead poisoning group showed collapse and glomerulosclerosis as well as tubular vacuolization and necrosis. In the 2.5 mg/kg manganese-treated group less tissue damage occurred. A significant increase in volume of kidney was observed in 2.5, 5 mg/kg manganese-treated and lead poisoning groups ($P < 0.05$). The number of glomeruli in 5, 10 and 20 mg treated manganese groups showed significant increase in compare to the lead poisoning group. Urea level in all groups under treatment with manganese ($P = 0.000$) and creatinine level in 2.5 mg treated manganese group were significant reduced in compare to those in the lead poisoning group ($P = 0.01$).

Conclusion: Treatment with 2.5 mg/kg and 5 mg/kg of manganese after injection of lead acetate for 14 days caused improvement in histopathology and biochemical signs of kidney tissue damage in mice.

Keywords: Lead, Kidney, Mice, Manganese

* Corresponding author. Tel: +98 515 7223028

Dr.paper57@gmail.com

Cancer cell detection using electrochemical nanobiosensor based on graphene / gold nanoparticle

Meisam Omid (Ph.D)^{*1}, Amir Yadegari (M.Sc)¹, Hakimeh Zali (Ph.D)², Mohadese Hashemi (M.Sc)¹ Hadi Hasanzadeh (Ph.D)⁴

1 – Dept. of Tissue Engineering and Regenerative Medicine, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical sciences, Tehran, Iran

2 - Proteomics Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3 - Faculty of New Science and Technology University of Tehran, Tehran, Iran

4 - Cancer Research Center and Dept. of Medical Physics, Semnan University of Medical Sciences, Semnan, Iran

(Received: 25 Nov 2015; Accepted: 15 May 2016)

Introduction: Nowadays, early cancer detection and effective treatment is crucial for improved prognosis and cancer management. In particular, the accurate qualitative detection of cancer cells represents a critical step in cancer diagnosis. **The aim of this study was to examine Cancer cell detection using electrochemical nanobiosensor based on graphene / gold nanoparticle.**

Materials and Methods: Modified graphene oxide/gold nanoparticle electrodes were employed to increase the sensitivity of human breast cancer MCF-7 cells detection, using CD44 biomarker. First the electrodes were modified with graphene, then gold nanoparticles were sediment on graphene-modified electrode. Then CD44 monoclonal antibody conjugated on the surface of gold nanoparticles, on graphene-modified electrode. Finally, the performance of the fabricated biosensors were investigated by using a common reference electrode composed of silver-silver chloride and a common platinum counter electrode at different antigen concentrations with the buffer and serum.

Results: The proposed electrochemical cytosensor delivered a high sensitivity with the average of 1.12 $\mu\text{A} / \text{cells ml}^{-1}$, and a low detection limit of 6 cells.

Conclusion: These results indicate that the cytosensor has great potential in diagnosis of cancers.

Keywords: Electrochemical nanobiosensor, Human breast cancer MCF-7 cells, CD44 Monoclonal antibody

* Corresponding author. Tel: ++98 21 22439848

m_omidi@sbmu.ac.ir

Effects of Kligman-Willis's triple combination therapy on quality of life in female melasma patients

Ramin Taheri (M.D)¹, Salman Asadi (M.D)¹, Narges Ghorbani (M.D student)², Raheb Ghorbani (Ph.D)^{*3}

1 - Kowsar Hospital, Faculty of Medicine, Seaman University of Medical Sciences, Semnan, Iran

2 - Seaman University of Medical Sciences, Semnan, Iran

3 - Social Determinants of Health Research Center, Department of Community Medicine, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran

(Received: 18 Jan 2016; Accepted: 23 Jul 2016)

Introduction: Melasma is common cause of skin hyperpigmentation. It's characterized by symmetric, irregular light brown to dark brown patches of hypermelanosis on parts of the body with most exposure to sun light. Melasma has a significant adverse impact on patients' quality of life (QoL). The aim of this study was to evaluate the effect of Kligman-Willis's formula treatment in female with melasma on their QoL.

Materials and Methods: In this study, 21 female patients, 15 or higher years old, referred to Semnan University of Medical Sciences (Semnan, Iran) dermatology clinic during 2013, were enrolled in the study. They were recognized with melasma for the first time. Treatment of patients with Kligman-Willis formula which contains 5% hydroquinone, tretinoin 0.1% and dexamethasone 0.1%, was done. This formula is a hydrophilic ointment base and is used topically. Treatment was continued for three months and the patients were instructed to apply the medication on the site of the lesion every night. Quality of life before and after 3 month treatment with Kligman-Willis's formula was investigated by DLQI (Dermatology Life Quality Index) questionnaire.

Results: Mean \pm SD age of the patients was 28.3 ± 7.2 years. Level of educational in 76.2% (n = 16) of patients was diploma or lower. 85.7% (n = 18) of patients were married. 85.7% of patients had lesion on the face. Before treatment, in 52.4 % of patients the skin disease had very large effect and in 47.6% of patients had extreme effect on QoL. Mean \pm SD score of DLQI before treatment was 20.29 ± 4.55 and after 3 months treatment decrease to 14.10 ± 3.94 , that was statistically significant ($p < 0.001$).

Conclusion: Findings showed that, treatment of melasma patients with Kligman-Willis formula based on a three-month period, would improve the quality of life of patients.

Keywords: Melanosis, Quality of Life, Hydroquinones, Tretinoin, Dexamethasone, Drug Combinations

* Corresponding author. Tel: ++98 23 33654367

r_ghorbani @ semums.ac.ir

Effects of different concentration of *Zattariamultiflora* essence on immunity system of broilers

Hamid Staji (M.Sc)^{1*}, Khosro Ghazvinian (M.Sc)², Ali Mahdavi (M.D)², Keivan Keramati (Ph.D)³

1 – Dept. of Pathobiology, Faculty of Veterinary Medicine, Semnan University, Semnan, Iran

2 – Dept. of Animal Sciences, Faculty of Veterinary Medicine, Semnan University, Semnan, Iran

3 – Dept. of Basic Sciences, Faculty of Veterinary Medicine, Semnan University, Semnan, Iran

(Received: 3 Apr 2016; Accepted: 20 Aug 2016)

Introduction: *Zattariamultiflora* (*Z. multiflora*) is a herb belonging to *Labiatae* family with known therapeutic effects, like anti-inflammatory and antimicrobial activity especially for gastrointestinal tract and respiratory systems and use of such herbs seems to be necessary in today's medicine. The aim of present study was to evaluate the effects of *Z. multiflora* essence on immunity of broilers.

Materials and Methods: Different concentrations of *Z. multiflora* were added to the food of broilers, then the antibody titer's were measured for Sheep Blood Cells (SRBC) and Newcastle Disease virus (NDV) plus stimulation rate of T-lymphocytes by Delayed-Typed Hypersensitivity (DTH) assay

Results: Assays revealed that addition of 200 & 400 ppm of *Z. multiflora* essence in the diet of broilers increased Ab levels against NDV, statistically ($p < 0.01$) and the Ab levels against SRBC in the group receiving 200 ppm of essence was increased ($p < 0.05$), while in the group receiving 400 ppm of the essence Ab levels against SRBC was decreased statistically ($p < 0.05$) in comparison to control group. Also in DTH assay, the skin thickening 48 hours post Ag challenge was higher statistically ($p < 0.05$) in the group receiving 200 ppm of the essence compared to control group, but in group receiving 400 ppm of the essence 48 and 72 h post Ag challenge, skin thickening was statistically lower ($p < 0.05$) than other groups.

Conclusion: The effects of *Z. multiflora* on immune system of broilers is dose dependent and use of lower concentrations of this herbal showed immunomodulatory properties. Thus, it is recommended to use the low concentrations of *Zattariamultiflora* in order to increase the resistance of broilers against enteric and respiratory infections.

Keywords: *Zattariamultiflora* essence, Humoral immunity, Cellular immunity, Broilers

* Corresponding author. Tel: +98 23 33654215

hstaji@semnan.ac.ir

Factors associated with preterm birth in Tehran province using multilevel logistic regression model

Saman Maroufizadeh (M.Sc), Reza Omani Samani (M.D)*, Payam Amini (M.Sc), Mahdi Sepidarkish (M.Sc)
*Dept. of Epidemiology and Reproductive Health, Reproductive Epidemiology Research Center, Royan
Institute for Reproductive Biomedicine, ACECR, Tehran, Iran*

(Received: 9 Apr 2016; Accepted: 2 Aug 2016)

Introduction: Preterm birth (PTB) is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health. The aim of the study was to determine the rate of PTB, and identify factors associated with it.

Materials and Methods: This cross-sectional study was conducted on 4419 pregnant women in Tehran province (Iran) from 6-21 July 2015. Data were collected by a researcher-made questionnaire through interview with mothers and review of their medical records. To identify factor associated with CS, two-level logistic regression model was used.

Results: The PTB rate was 5.6% in this study. In univariate analysis, mother's age, preeclampsia, Caesarian section, multiple pregnancies, and use of ART were significant factors of PTB. Moreover, multivariate analysis has shown a significant relationship between PTB and preeclampsia, multiple pregnancies and use of AR. In multivariate analysis, mother's age had a positive impact on PTB, but this relationship was not statistically significant ($p=0.051$). The intra-class correlation (ICC) between hospital is 0.208 indicating approximately 21% of the total variation in the response variable accounted for by the hospital.

Conclusion: According to the results, factors such as preeclampsia, multiple pregnancies and use of ART were associated with PTB. Therefore, it seems that these factors can be effective in determining the risk in neonates and providing factors in reducing mortality.

Keywords: Preterm birth, Risk factor, Pregnancy, Infant, Multilevel logistic regression

* Corresponding author. Tel: +98 21 22339929
samani@royaninstitute.org