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Oocyte Quality & its Impact on the Reproductive Outcomes of Women Undergoing Assisted Reproduction: A Review

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Abstract

The Assisted Reproductive Technology (ART) has led to technical advancements in the last few years. These techniques have greatly assisted in achieving an acceptable pregnancy rate. Pregnancy followed by delivery signifies the success of an ART treatment. The success rate of an ART treatment is hinged on various parameters of which oocytes have a primary role in fertilization, early embryo development and its subsequent implantation. Successful pregnancies are common in assisted reproductive technology clinics because of invasive and non-invasive methods used to isolate biologically competent oocytes. The process of fertilizing the embryo, early embryo growth, implanting of the fertilized embryo, and favorable pregnancy results may be predicted by morphological features like zonapellucida, the cumulus complex, first polarized body, perivitelline membrane area space, spindle formation assembly, and ooplasm. The non-invasive assessment of oocyte quality based on cumulus gene expression analysis in conjunction with morphology assessment can improve the clinical pregnancy (CPR) and live birth rates (LBR). The infertility that is linked with poor oocyte quality may be explained by a number of different processes that are not exclusive to one another. To a large extent, the success of in vitro fertilization (IVF) depends on the oocyte, which plays a critical role in defining embryonic competence. It has been suggested in research studies that the shape of oocytes may serve as a non-invasive indicator of the quality of the oocytes. The current review investigates the correlation of oocyte quality and its effect on the clinical outcomes of women undergoing regulated ovarian stimulating for an intracytoplasmic sperm injection (ICSI).

Keywords: Embryo, Pregnancy, In-vitro fertilization, Endometriosis, Polycystic ovarian syndrome.

INTRODUCTION

Extending endometrial or stroma tissues beyond the uterine cavity is a diagnostic criterion for endometriosis.[1] Women of reproductive age (10–15%) and those receiving infertility treatments (25%–50%) might be affected. The American Fertility Society's grading system for the severity of the condition, which is based on the outcomes of laparoscopic procedures, is extensively utilized

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by practitioners. However, when it comes to characterizing severe endometriosis, this anatomical categorization falls short. There is just a weak relationship between this and the level of the patient's symptoms, and it is not a good predictor for whether a pregnancy would occur naturally or be induced. Endometriosis may manifest itself clinically in a wide variety of ways, and these variations have been attributed to a wide range of pathophysiological mechanisms.[1] Most clinicians like to entertain many hypotheses. Genetics, hormones, immunology, angiogenesis, and the environment have all been demonstrated to have a role in the development of endometriosis.[12] Oocyte size has been proposed as a non-invasive indicator of oocyte quality in certain published works.[1] Some morphological flaws, detectable with a light microscope, were linked to poor oocyte quality by Tus, Van Blerkom, and Henry.[7] Cumulus cells, nucleus development, and cytoplasmic and extra-cytoplasmic features are examined to establish oocyte morphology.[1] Polycystic ovary syndrome (PCOS) is diagnosed in almost a quarter of infertile couples, and its incidence in asymptomatic people is estimated at 33%.[12,13] The endocrine, metabolic, and reproductive systems are all affected by polycystic ovary syndrome[14], making it a complicated multi-spectrum illness. The hyperandrogenic condition in PCOS is the root cause of decreased folliculogenesis.[15] The most frequent non-invasive evaluation techniques are now focused on the morphology and developmental parameters of embryos during in vitro development.[16] Only around 5% of new oocytes result in a live-born kid, according to a clinical investigation that evaluated the true biological effectiveness of IVF by measuring the percentage of live births in proportion to the number of oocytes extracted.[18] Because gonadotrophins increase the number of follicles and accessible oocytes, they have significantly improved the success rate of in vitro fertilization.[19] By stimulating ovarian follicles, retrieving follicular fluid, and isolating and vitrifying mature oocytes, the method is known as oocyte cryopreservation (OC).[20]

Over the past few years, there has been a decline in the number of individuals across the globe that has difficulties with reproduction. PCOS is a potential cause of anovulatory infertility, however, it is treatable. The layer of pellucid zonal, polarized body formation, cumulus-oocyte, and the internal features of oocytes have all been connected to the process of fertilizing the embryo, formation of cleavages and splits in the embryo, and the development of the outcomes of the process of embryo fertilization clinically in the ART Laboratory.[2] Oocyte chromatin aligns in metaphase two (MII) in the equatorial region of the meiotic spindles (MS).[2] Infertile women with polycystic ovary syndrome (PCOS) have two assisted sexual treatment options: controlled ovarian hyperstimulation (COH) and in vitro maturity (IVM) therapy. The increasing global incidence of infertility may be attributed to several causes, including older mothers and the stresses of contemporary life. For this reason, ART's significance grows constantly. Although ART has improved in efficiency and accuracy, the success rate is still only about 35% when measured by the number of live births per transplanted embryo.[4] PCOS is a hormonal disorder that mostly affects reproductive-aged women. The Rotterdam criteria for PCOS involve the presence of medical and/or quantitative hyperandrogenism, ovarian dysfunction, and polycystic ovary shape (PCOM). Nearly a quarter of couples who are infertile are diagnosed with the polycystic ovarian syndrome (PCOS), and its occurrence in asymptomatic persons is put at 33%.[5] Embryos that were developed in vitro have not shown the same potential for attachment as embryos that matured in vivo. This is because a healthy kid is more likely to grow from an egg that has been allowed to mature in vivo. The poor growth of embryos observed in in vitro developed human oocytes has been linked to a failure to synchronize the process of maturation in the cytoplasm and the nucleus of the developing and growing embryo. While the relationship between metaphase II (MII) ovarian shape and the success of the process of fertilization taking place in vitro is well established in conventional IVF, it is less clear after sperm injection taking place intracytoplasmic-ally (ICSI). Only two of the studies found any connection between morphologic abnormalities and the fertilization and quality of the embryos produced by ICSI. Despite good fertilization, embryo quality, and live birth rates, oocytes with cytoplasmic abnormalities have been shown to have a lower implant rate and a lower rate of sustained pregnancy.[6] It has been discovered that the shape of the first polar body and other extracytoplasmic abnormalities observed at the time of ICSI are accurate indicators of subsequent development and embryo quality. Furthermore, it has been found that the elective transplanting of eggs selected based on these features has been linked to higher implanting and pregnancy rates. These studies show that aberrant MII oocytes have a reduced likelihood of the process of fertilization cleavage and embryonic viability compared to

normal oocytes. The morphology of MII oocytes generated in vitro has not been studied before.[6] In vitro fertilization (IVF) has been around since 1978, when the first kid conceived with the help was born. Since that time, ART has expanded considerably, resulting in the birth of over 8 million children with the use of IVF across the world.[21]

Significant progress has been made in the field of human-assisted reproductive technology in recent decades, from in vitro ovarian maturation and fertilization through animal cloning. In general, the scientific literature agrees that oocyte quality is the most important factor in determining successful fertilization, initial growth, and implantation. Therefore, the success of infertility treatment operations may depend on several factors, the most important of which is the quality of the oocytes used in the processes. This study set out to do just that, reviewing the tools and standards used to evaluate oocyte quality morphologically.[23] Recent decades have seen extensive research into assisted reproductive technology for humans, leading to substantial progress in this field. This includes anything from the maturation and implantation of oocytes in vitro to the cloning of animals. The quality of the oocytes is the single most important factor in determining the success of fertilization, early growth, and implantation, according to the research. Consequently, the success of treatment for infertility treatments may depend on several factors, the most important of which is the quality of the oocytes used in the operations. The purpose of this study was to provide a comprehensive overview of the techniques and standards currently in use for morphologically evaluating oocyte quality.[24]

Numerous studies have examined the correlation between oocyte excellence, embryo growth, and successful in vitro fertilization, also known as IVF.[23] When choosing embryos for transfer, morphology is used almost entirely by most IVF clinics, including ours. Our weekly examination of unsuccessful IVF cycles has shown that oocyte evaluations are often more predictive of IVF success than embryo evaluations. We postulated that oocyte-level prediction of pregnancy success, rather than embryo-level prediction, could provide more useful information when choosing embryos for transfer. Future perspective research was created to examine this hypothesis. The quality of the embryo is now the strongest predictor of a successful pregnancy; hence researchers have focused nearly entirely on enhancing embryo evaluations rather than oocyte evaluations. This has recently led to a rise in the use of high-priced closed robotic incubation systems that rely on time-lapse imaging.[23] Taking into account the exorbitant price of IVF, it makes sense financially to choose embryos more efficiently. Consequently, we prospectively studied a new, simple oocyte scoring method and contrasted it to the older, more widely used day 3 embryo evaluations currently used by the majority of IVF clinics.[23]

Assessment of the quality of the oocyte required further for the AZT technique:

Oocyte and embryo classification was the subject of a 2011 meeting of experts. These previously established guidelines are now being updated to account for new information and technological capabilities. The progression of the oocyte's nuclei & and cytoplasm is directly linked to the formation of a human embryo. Oocyte quality has been hypothesized to be reflected in cytoplasmic characteristics such as cytoplasmic homogeneity, the presence of vacuoles, and the formation of smooth clumps of the endoplasmic reticulum.[8] There have also been suggestions about extracytoplasmic characteristics, such as the initial polarized body form, perivitelline temporal dimensions, zonapellucida failures, and shape.

Factors affecting oocyte quality

Factors including smoking, alcohol usage, obesity, a woman's age, endometriosis, assisted reproductive technology (ART), and genetic abnormalities like hormone receptor polymorphisms may all have a detrimental impact on oocyte quality. Biochemical and morphological alterations in oocytes have been linked to a rise in ROS, or reactive oxygen species, a type of oxygen, which may occur as a result of systemic diseases. Oocyte dysmorphism may manifest internally or externally in the cell. Preimplantation testing development failure is proportional to the degree and number of oocyte morphological abnormalities. The lady had four rounds of IVF, all of which resulted in dysmorphic oocytes. Aiming to connect the dots between the oocyte characteristics stated in the case reports aboutthe authenticity of the oocyte and the size reported in the study cited in the review, this literature review seeks to conclude the nature of these connections.[9]

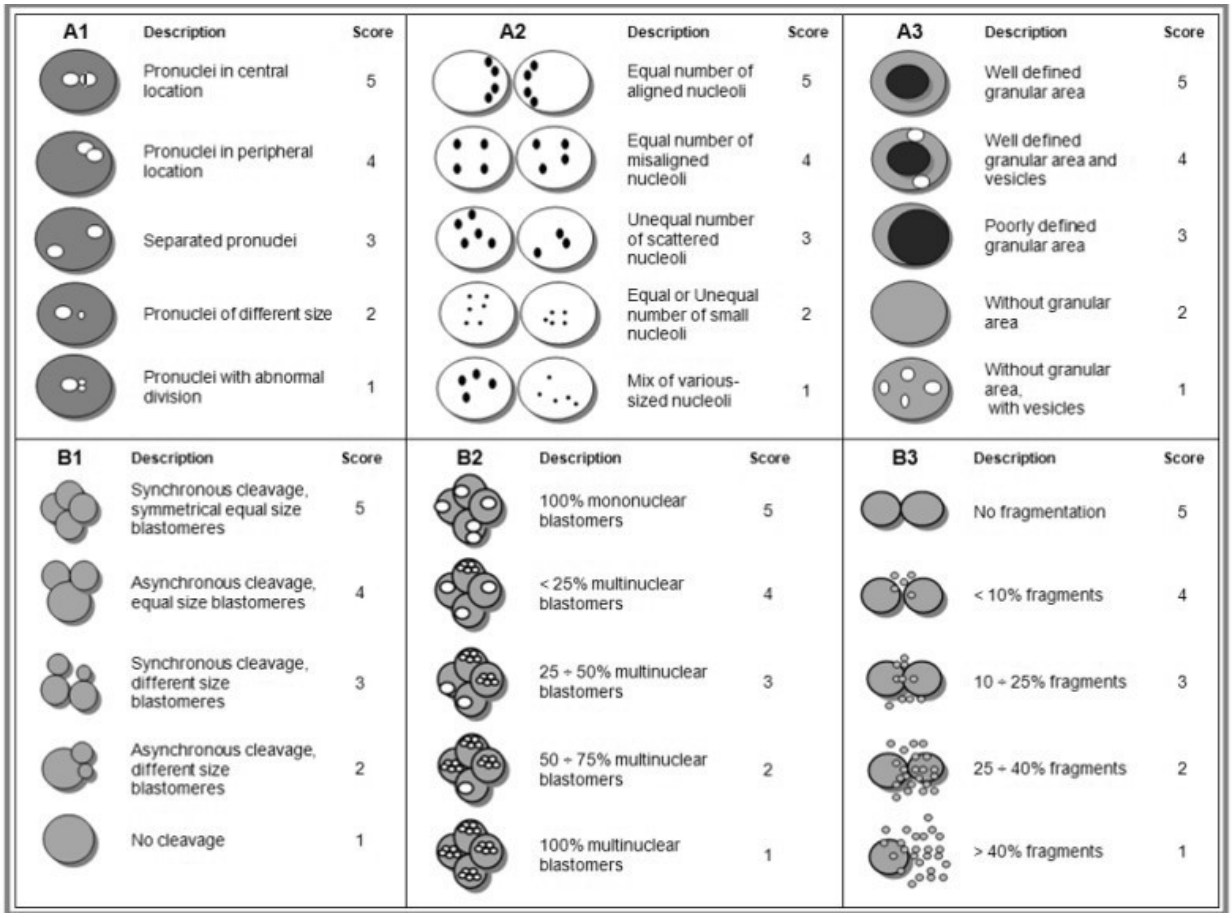


Fig. 1: shows the different oocyte assessment methods[22]

Table 1: Shows the grading system for oocytes[25]

Grade	Rating	Description
		<10%fragmentation
1	Good	Stage-specific cell size
		No multinucleation
		10 – 25% fragmentation
2	Fair	Stage-specific cell size for majority of cells
		No evidenceof multinucleation
		Severe fragmentation (.25%)
3.	Poor	Cell size not stage specific
		Evidence of multinudeation

Pregnancy outcomes related to the use of the technique of assisted reproductive technique

The proportion of live births that may be attributed to fresh embryo transfers, which includes cycles of IVF and ICSI, climbed from 33.3% in 2007 to 36.5% in 2009. This is a significant increase. The abortion rate per implantation averaged 5.3% between 2007 and 2009. Only 2.5% of all live births that followed fresh embryo transfer (including those that followed IVF and ICSI) were ectopic. This value didn't alter at all during the course of the study's three years. The incidence of ectopic pregnancies is much lower than the globally estimated rate of 2% per recorded pregnancy. The rates of multiple births were also calculated. About 74% of births were to a single mother during the research period, whereas 22% were to a set of parents. Statistics on the prevalence of preterm and full-term births, as well as perinatal illness and death, were not provided. The number of cycles when frozen embryos were transferred after being artificially treated with hormones rose between 2007 and 2009. Matching years' numerical sums grew from 1525's to today's 2678's. The percentage of women who waited for their menstrual cycle to begin before preparing for an embryo freeze transfer (FET) fell from 45% in 2007 to 27% in 2009. Using exogenous hormones to stimulate the endometrium's natural maturation process eases physicians' concerns about using synthetic cycles. The total amount of FET cycles increased from 1954 to 3087 between 2007 and 2009. From 2007 to 2008, the proportion of FET cycles in which just one

embryo was transplanted fell from 9.46% to 7.87%. The number of women using donor eggs, whereby oocytes are obtained from strangers, doubled from 2007 and 2009. From 1047, we are now 2130 strong. There was only a 20% rise in the number of eggs donated by known or related donors. The rise in media attention given to organizations that popularized the field of reproductive technologies for assisted living may explain why customers prefer anonymous donors: more women may come forward to offer their services as skilled donors in exchange for financial payment. It is not known how frequently one donor may provide oocytes to many recipients.[11]

Women around the age limit of 45 made up the bulk of egg donors' recipients. There was a consistent pattern over all three years. In the study, women aged 55 and above made up around 1.18 percent of the egg recipients. Better techniques for tracking patients for health risks like diabetes, hypertension, as well as coronary heart disease have contributed to the recognition that conception in the postmenopausal group of women may be unphysiological, potentially endangering the health of the mother. That's why a lot of docs advise against becoming pregnant beyond 50.[11]

CONCLUSION

When assessing physical characteristics, some ART clinics utilize light or polarized microscopes. As a consequence, this has the potential to aid in the choosing of high-quality oocytes, a step crucial to enhancing the rate at which healthy infants are born. Meiotic spindle, the amount of cyclin-dependent kinase (CDK) activity, cyclin-dependent phosphatase (CPP) activity, vacuoles/refractive organizations, oocyte shape, granulation, which and ooplasm viscosity are among oocyte morphologies that are routinely examined. For oocyte selection, it is unclear which of these variants is optimal. Using a mix of morphological evaluations, it may be feasible to reliably predict which oocytes will end up incapable of early embryos. Oocytes with obvious or slightly fragmented cytoplasm, a small PS, a presumably intact PB, typically apparent meiotic spindle-like as well as CC, and colorless as well as birefringentZonapellucida ought to be chosen for the initial administration of ARTs in the absence of additional constraints like the age of the patient, collected oocyte numerals, or previous ART failures. Particularly important is the evaluation of these morphological parameters in an extensive group of similar patients across a wide variety of ART centers.[10]

Predictions of oocyte quality might be improved by combining morphological studies with modern technologies like as genome sequencing, transcriptomics, proteomics, and metabolomics. Selecting embryos with desirable physical characteristics and, in certain situations, genetic testing before implantation for aneuploidy testing might increase the success rate of fertility treatments such as fertilization taking place in-vitro and injection of sperm (IVF/ICSI) taking place in an intracytoplasmic way and procedures to reduce the occurrence of multiple embryos during pregnancy. Early embryos are being tested for desirable morphological, metabolism, proteomic, epigenetic, and genome characteristics. In circumstances where a relatively small amount of oocytes may be retrieved owing to poor fertility or regulatory limits, morphological features for choosing competent oocytes may still be employed despite their lower therapeutic effectiveness than first envisaged.[10]

REFERENCES

1. Bulun SE, Yilmaz BD, Sison C, Miyazaki K, Bernardi L, Liu S, *et al.* Endome- triosis. Endocr Rev. 2019; 40(4):1048-79doi: 10.1210/er.2018-00242Pubmed:30994890.
2. Asa E, TabatabaeeRM, Farrokhi A, NejatbakhshR. Relationship between meiotic spindles visualization and intracytoplasmic sperm injection outcomes in human oocytes. AnatCell Biol. 2017; 50(1):26-6doi: 10.5115/acb.2017.50.1.26.
3. Liu T, Liu D, Song X, Qu J, Zheng X, Li J, *et al.* Lipid metabolismwasassociatedwithoocyte in vitro maturation in womenwithpolycysticovariansyndromeundergoingunstimulatednaturalcycle. Front CellDevBiol. 2021;9:719173doi: 10.3389/fcell.2021.719173Pubmed:34540838.
4. Lemseffer Y, TerretME, Campillo C, Labrune E. Methods for assessingoocytequality: areview of literature. Biomedicines. 2022; 10(9):2184doi: 10.3390/biomedicines10092184Pubmed:36140285.
5. Nikbakht R, Mohammadjafari R, Rajabalipour M, Moghadam MT. Evaluation of oocyte quality in polycystic ovary syndrome patients undergoing ART cycles. FertilRes Pract. 2021;7(1):2doi: 10.1186/s40738-020-00094-zPubmed:33397466.
6. Mikkelsen AL, Lindenberg S. Morphology of in-vitro matured oocytes: impact on fertility potential and embryo quality. HumReprod. 2001; 16(8):1714-8doi: 10.1093/humrep/16.8.1714Pubmed:11473970.
7. Van Blerkom J, Henry G. Oocyte dysmorphism and aneuploidy in meiotically mature human oocytes after ovarian stimulation. Hum Reprod.1992;7(3):379-90doi: 10.1093/

oxfordjournals.humrep.a137655Pubmed:1587948.

8. Latif S, Saridogan E. Endometriosis, oocyte, and embryo quality. J ClinMed.2023;12(13):4186doi: 10.3390/jcm12134186Pubmed:37445220.
9. Guimarães RMGC, Ribeiro LM, Sasaki LP, Nakagawa HM, Cabral IO. Oocyte morphology and reproductive outcomes - case report and literature review. JBRA Assist Reprod.2021;25(3):500-7doi: 10.5935/1518-0557.20210001Pubmed:33739798.
10. Ozturk S. Selection of competent oocytes by morphological criteria for assisted reproductive technologies. MolReprodDev.2020;87(10):1021-36doi: 10.1002/mrd.23420Pubmed:32902927.
11. Malhotra N, Shah D, Pai R, Pai HD, Bankar M. Assisted reproductive technology in India: A 3 year retrospective data analysis. J Hum ReprodSci.2013;6(4):235-40doi: 10.4103/0974-1208.126286Pubmed:24672161.
12. Murphy MK, Hall JE, Adams JM, Lee H, Welt CK. Polycystic ovarian morphology in normal women does not predict the development of polycystic ovary syndrome. J ClinEndocrinolMetab. 2006; 91(10):3878-84doi: 10.1210/jc.2006-1085Pubmed:16882750.
13. Sigala J, Sifer C, Dewailly D, Robin G, Bruyneel A, Ramdane N, *et al*. Is polycystic ovarian morphology related to a poor oocyte quality after controlled ovarian hyperstimulation for intracytoplasmic sperm injection? Results from a prospective, comparative study. FertilSteril. 2015; 103(1):112-8doi: 10.1016/j.fertnstert.2014.09.040Pubmed:25450303.
14. Lizneva D, Suturina L, Walker W, BRakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycysticovarysyndrome. FertilSteril. 2016; 106(1):6-15doi: 10.1016/j.fertnstert.2016.05.003Pubmed:27233760.
15. Catteau-Jonard S, Dewaily D. Pathophysiology of disturbedfolliculogenesis in PCOS. Med Reprod. 2009; 11(3):191-7 doi: 10.1684/mte.2009.0241.
16. ScottL.Thebiologicalbasisofnon-invasiveStratergies for selection of humanoocytes and embryos. Hum Reprod Update. 2003; 9(3):237-49doi: 10.1093/humupd/dmg023Pubmed:12859045.
17. Sayutti N, Abu MA, Ahmad MF. PCOS and role of cumulusgeneexpression in assessingoocytesquality. Front Endocrinol. 2022; 13:843867doi: 10.3389/fendo.2022.843867Pubmed:35721714.
18. Patrizio P, Sakkas D. From oocyte to baby: a clinical evaluation of the biological efficiency of in vitro fertilization. FertilSteril. 2009; 91(4):1061-6doi: 10.1016/j.fertnstert.2008.01.003Pubmed:18325517.
19. Magaton IM, Helmer A, Eisenhut M, Roumet M, Stute P, von Wolff M. Oocyte maturity, oocyte fertilization and cleavage-stage embryo morphology are better in natural compared with high-dose gonadotrophin stimulated IVF cycles. ReprodBiomed Online. 2023; 46(4):705-12doi: 10.1016/j.rbmo.2022.11.008Pubmed:36754739.
20. Han E, Seifer DB. Oocyte cryopreservation for medical and plannedindications: A practicalguide and overview. J ClinMed. 2023;12(10):3542doi: 10.3390/jcm12103542Pubmed:37240648.
21. FauserBC. Towards the global coverage of a unified registry of IVF outcomes. ReprodBiomed Online. 2019; 38(2):133-7 doi: 10.1016/j.rbmo.2018.12.001Pubmed:30593441.
22. Stamenov G, Parvanov D, Chaushev T, Baltadzhieva D, Iliev I, Dzhambazov B. Approaches for prediction of the implantation potential of human embryos. J BioSciBiotechnol. 2013; 2:79-88.
23. Lazzaroni-Tealdi E, Barad DH, Albertini DF, Yu Y, Kushnir VA, Russell H, *et al.* Oocyte Scoring Enhances Embryo-Scoring in Predicting Pregnancy Chances with IVF Where It Counts Most. Plos One. 2015; 10:e0143632.
24. Lasiene K, Lasys V, Glinskyte S, Valanciute A, Vitkus A. Relevance and methodology for the morphologicalanalysis of oocytequality in IVF and ICSI. J ReprodStem Cell Biotechnol. 2011;2(1):1-13doi: 10.1177/205891581100200102.
25. Halim B, Lubis HP, Novia D, Thaharuddin M. Does oval oocyte have an impact on embryo development in in vitro fertilization? JBRA AssistReprod. 2017; 21(1):15-8doi: 10.5935/1518-0557.20170005Pubmed:28333026.