**The Risk of Congenital Autism in Using Paracetamol during Pregnancy**

**LITERATURE REVIEW**

**2.1 Introduction**

Paracetamol use is very popular with expectant women globally as a pain reliever (Brandlistuen et al., 2013). Also known as Acetaminophen it is readily available in many countries over the counter basis and has been branded by many researchers as a safe drug to be used by the pregnant women during their period of pregnancy. Schaefer et al., (2008, p.37) classifies paracetamol as a nonteratogenic drug meaning that it does not affect congenital neurodevelopment processes of an individual. On the other hand, teratogenic drugs have adverse effects on a neonatal neurodevelopment processes (De Santis et al., 2004). Conversely, other studies indicate that paracetamol intake during pregnancy may elevate the risk of autism in the child (Moody, 2016). Autism is a developmental disorder associated with neurodevelopment and manifested by communication and socialisation strains in affected persons (Bienkowski, 2016). It is common globally. However many scientists continue to dispute the possibility of the link between autism and paracetamol in pregnancy (Bulman, 2016). Various research studies have indicated the use of paracetamol and its exposure over a range of 45-65%, especially during the gestation period (Shaw, 2013). Use of paracetamol risks the exposure involving inflammatory as well as immunologic strategies, and they are prone to expose the patients to predisposed oxidative stress. The effects of paracetamols are claimed to have more impact on boys than girls though it affects attention in both sexes (Thomas, 2016). Alongside these effects and others, there are several hypotheses developed which indicate that they expose the foetus as well as compromise the neurodevelopment of the foetus especially in the brain (Andrade, 2016). Of the ecological studies developed, there is a development that there is a population trend which shows that there is a constant population level involved with the use of paracetamol which has elevated the case of autism with one of the research examining the use of paracetamol during pregnancy (Andrade, 2016). However such claims are still contentious and there is still no consensus on whether or not paracetamol intake during pregnancy may lead to congenital autism.

One of the research done on the use of paracetamol by pregnant women showed that when it is used for over 28 days it pointed out to having various motor delays as well as impairments with a case of hyperactivity experienced when the child is at the age of 3 years (Andrade, 2016). However, according to the research, the emotional and social behaviours of the children were not affected. Another group of researchers determined that, after a follow-up of 12 years and seven months, got results that the parents who were exposed to paracetamol during the gestational period was directly related to a case of autism but this case was only limited to the cases where the hyperkinetic disorder was present (Pickles, 2016). With the pre-existing data about the risks of use of the paracetamol during gestation period presents a subsequent risk to the mother concerning attention deficit as well as to the child resulting from autism (Whiteman, 2016). Nevertheless, the extent of such risks has not been ascertained satisfactorily.

In other researches done, the case of autism is highly disapproved indicating that autism is only evident to boy child in the developmental stages and only the attention deficit symptoms and hyperactivity symptoms are present in both genders as a result of the use of paracetamol (Dietert et al., 2011). Research published in the International Journal of Epidemiology for a Spanish company developed the theses by indicating that the children exposed to paracetamol had a 30% increase in the risk of the detriment to certain particular actions as well as an increased risk of the autism symptoms especially for the boys (Whiteman, 2016). It seems like male neonates are more susceptible to autism causing impacts of paracetamols (Macrae & Hagan, 2016). Although the research was unable to indicate the exact amount of tablets used by the mothers, the rating of either never or sporadic or frequent was utilized by the Spanish researchers to determine the extremity of the actions of the intake paracetamol and thereby relate them to the evident cases of autism and cognitive behaviours (Whiteman, 2016).

Concisely it is evident that there is no solid position as to whether or not the use of paracetamol during pregnancy can actually trigger congenital autism considering that other studies only claim that such an incidence only occurs to boys and not girls. This study therefore seeks to establish the correlation between the functioning of paracetamol and neurodevelopment in a foetus in relation to autism.

**2.2 Paracetamol and Neurodevelopment**

As foetus, children who were exposed to paracetamol, which is taken by the pregnant mother at the time they are pregnant at a percentage rated as 30% higher, compared to those children whose parents do not take the pills (Dietert et al., 2011). According to research, the children who are exposed to use of paracetamol consistently tend to perform more badly on the tests done by computers concerning the rate of attention, the impulse build-up, and the processing activity of the person in context. There are varieties of reasons why paracetamols pose harm to the process of neurodevelopment, which is discussed below.

***2.2.1 Why Paracetamol are harmful to neurodevelopment***

The paracetamol intakes by pregnant women act on relieving pain by action on the cannabinoid receptors, which are located in the brain thereby increasing the case of autism. The receptors assist the body in determining the process and steps in which the neurones are supposed to mature and how they interconnect with each other (Schaefer et al., 2007, p.10). Therefore, paracetamols can affect this development

The paracetamols can further affect how the immune system performs and develops, and therefore the paracetamols may influence the cognitive evolution of the child owing that the child does not have the cognitive ability to metabolise the contents of the drugs thereby leading to a case of autism (Schaefer et al., 2007, p.10). It could be the possible basis of association of paracetamol with congenital autism.

However, many of the scientists have recommended that there should be more studies conducted so that there can be a correct solution on the exact amount of paracetamol which the pregnant mother can take without causing harm or damage to the child (Dardennesa et al., 2011). With such recommendations, scientists believe that paracetamol can have greater positive effects as compared to the defined adverse consequences (De Santis et al., 2004). However, such arguments are also without scientific disapproval of the possible role of paracetamols in congenital autism.

In a particular research, mothers were analysed on the use of paracetamol during their pregnancy with a classification of rare medium and frequent. From the results, the analysis showed that 43 percent of the children had been exposed to paracetamol, for those diagnosed at age one, and 41 percent for those at age five (De Santis et al., 2004). The exposure to paracetamol was mainly during the first 32 weeks of pregnancy for all the children evaluated. Concisely the foetus undergoes formative neurodevelopment at this stage.

***2.2.2 Insufficient Evidence***

According to a variety of researchers, there is no sufficient proof of as to whether paracetamols cause autism and the research done by various scholars have been highly disputed by some of the top-notch doctors (Källén et al., 2013). According to Dr James Cusack, the research papers do not sufficiently support the link between the use of paracetamols and the representation of autism among children. Dr James believed that the results presented by the study were just preliminary results which did not fully support the actions shown by the use of paracetamol and therefore should not be a concern to the pregnant mothers whatsoever. In support of this, Dr James indicated that the environmental factors, which have been associated with autism do not in any way seem congruent to the deductions of the study. In retrospect, it is impossible to dispute that the both the environment and genetics play a significant role in the aetiology of the disease (Ornoy et al., 2016).

In study aimed at examining and determining as to whether the paracetamol used by the pregnant mother affected the child case of developing autism at the age of five years, the prenatal paracetamol used by the parents was recorded over a spaced time of three telephone interviews. A set of trained psychologists were able to test the reception of the children who were exposed to use of paracetamol by employing the Test of Everyday Attention for Children at Five (TEACh-5) strategy. In the research, the scholars identified that within the starting trimester, there was a development of poor concentration result from the child indicating a mean difference of approximately -0.34 as well as a 95% confidence rate or interval (Liew et al., 2015). The number of children who were prenatally exposed to the use of paracetamol was also identified to have an abnormal overall attention as well as poor scores in the particular attention difficulties. However, apart from suspecting the use of paracetamol only, it may be necessary to identify other possible underlying issues. The associated elevated risk of reduced attention from the children indicated that there was a progressively increased risk of the children getting a higher risk of congenital autism in case the parents increased the use of paracetamol during pregnancy (ESHRE Capri Workshop Group, 2014).

**2.3 Autism Effect and Anxiety**

Nervousness is a standout amongst the most widely recognised reasons why those with the condition look for support from wellbeing experts. As of recently, it was not clear what activated it - however, another review cases to have found an answer (Sivojelezova et al., 2005). Analysts say high amounts of tension can be clarified by extremely introverted individuals' trouble in recognising and understanding their feelings. Thus, they recommend exercises, for example, care could be especially viable - and even upset the treatment of nervousness in a mental imbalance.

'The male mind might be more helpless against hurtful impacts amid early life,' she said (ESHRE Capri Workshop Group, 2014). The review inferred that the far-reaching presentation of newborn children to paracetamol in the womb could expand the number of kids with ADHD or extreme introvert-related range of range side effects. In any case, their research focused on a generalised perspective. However, further reviews ought to be led with more accurate dose estimations, and that the dangers versus advantages of paracetamol use amid pregnancy and early life ought to be surveyed before treatment suggestions are made (Amundsen et al., 2015, p.2). The preparatory outcomes from this review recommend that incessant paracetamol use all through pregnancy may affect consideration work and somewhat increment the danger of hyperactivity in the posterity at matured five years of age. 'No impact on psychological, engine or social advancement was distinguished.'

'Future reviews ought to consider measurements and also other conceivable contributory variables. 'Be that as it may, ladies ought not to be frightened by the after-effects of this review, and we prescribe that pregnant women keep on following current direction and take the most minimal robust measurement for the briefest conceivable time when necessary (Guttuso et al., 2014). 'On the off chance that the suggested dosage of paracetamol doesn't control side effects or torment, look for exhortation from your birthing assistant, GP or obstetrician. Another review, in any case, proposes that it may be no overall protection in the wake of recognising a connection between pre-birth presentation to the medication and indications of a mental imbalance and consideration shortage hyperactivity issue (Prandota, 2011). While the analysts can't pinpoint the correct instruments by which pre-birth acetaminophen presentation might be connected to extreme introvert traits or ADHD, they take note of that the medication eases torment by focusing on cannabinoid receptors in mind, which can decrease availability between nerve cells.

**2.4 Ecological Link**

The ecological relation of autism disorder and use of paracetamol and the interrelation with the neurological development is another study performed by another group of scholars (Rusu et al., 2015, p.901). In this case, the researchers identified that susceptibility is associated with a connection between the genetic heritability as well as associated environmental factors, which affect the person in context (Schaefer et al., 2008, p.38). The issue of the synchronous advancement of cases of autism as well as the use of paracetamol in relation to the diverse biological plausibility is having led to hypotheses developed by scholars who indicate that the use of paracetamol increases case of autism. In determining the relationship between the prenatal exposures of the parents to paracetamol, the aspect of prevalence rate was employed to determine the development of research and usage of the paracetamol by the parents. Unfortunately, the aspect of levels of intake is still not yet verified.

Paracetamol is a standout amongst the most widely recognised antipyretic pain relieving pharmaceuticals around the world. In 1980, after adequate confirmation a relationship arose amongst salicylates and Reyes disorders. Paracetamol supplanted headache medicine as the necessary medication for in pregnant women and kids. Since that date, paracetamol utilisation all through the world has expanded. Despite the fact that commonness in information for extreme introvert traits and ASD are of indeterminate exactness, many carers report stable increments in pervasiveness over this same day and age (Rusu et al., 2015, p.901).

***2.4.1 Prenatal Exposure Trends***

Past research has distinguished paracetamol utilisation inclines that inquisitively match with the ascent in commonness and populace socioeconomics of a mental imbalance/ASD. In the US Slone, the study of disease transmission Centre Birth Surrenders think about paracetamol was the most frequently utilised medicine among all subjects with use higher amid pregnancy than before pregnancy whereby the scene would likely build the introduction to paracetamol (Blecharz-Klin et al., 2015).

In the U.S., use of paracetamol by pregnant women reflects the populace socioeconomics of women whose youngsters create a mental imbalance range issue, by race, age and training (Andrade, 2016). The populace socioeconomics for mothers who circumcise their children is likewise fundamentally the same as, with rates expanding with financial status and protection scope rates (Avella-Garcia et al., 2016). Things that have demonstrated that a parent's own particular utilisation rates of paracetamol and different medicines correspond with what they provide for their youngsters, so a comparable statistic use example would be standard for youth presentation (Andrade, 2016). This contemporary U.S. example might be suggestive of an added substance nature of both pre-birth and early life performance to paracetamol and a relationship to last introverted traits/ASD.

***2.4.2 Early Life Exposure Behaviour***

With all the drugs that are available, Paracetamol is considered the most widely recognised medication regulated to US kids and the overwhelming pain relieving/antipyretic medication among children who have reached 24 months. Paracetamol is proposed for agony administration taking after immunisations. In 1983, the average U.S. child got 8 inoculations up to the period they reached 2 years old. A research in 2011, the normal was 25, a 313% expansion (Bauer & Kriebel, 2013). Consequently, considering the state of the immediate speculation, these speak to expanded open doors for paracetamol presentation in torment administration (in spite of the fact that overseeing a few immunisations on the second means absence of pain may not increment relatively) (Bauer & Kriebel, 2013).

A current review speaking to one-fifth of all paediatric doctor's facility confirmations in the U.S. Hospitalization of youngsters and neonates for contamination and non-irresistible ailment have been related to the expanded danger of ASD in a substantial Danish associate [risk proportions 1.38 (95% CI: 1.31 to 1.43) and 1.76 (95% CI: 1.68 to 1.86), separately] (Avella-Garcia et al., 2016). It is important to note that there is no substantive information why the gender disparity in paracetamol associated congenital autism may occur.

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