

# Maternal Use of Methadone and Neonatal Thrombocytosis

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## Citation

M Kasem, A Sayasneh, N Matta. *Maternal Use of Methadone and Neonatal Thrombocytosis*. The Internet Journal of Pediatrics and Neonatology. 2008 Volume 11 Number 1.

## Abstract

**Objectives:** To identify the relationship between the maternal use of methadone and early neonatal thrombocytosis. **Methods:** All babies in our study were born at Princess Royal Maternity Hospital in Glasgow between 01/2006-01/2007 inclusive. FBC for both the study and the control groups were performed for different indications during the first week of life (jaundice, jitteriness, maternal prolonged rupture of membranes, maternal positive HVS for GBS, or maternal pyrexia). Only babies who were full term at delivery, with normal CRP ( $<1$ ), and negative blood culture (no bacterial growth) were included in the study. **Results:** 181 babies were born to methadone users. 62 babies fulfilled the criteria of the study. 119 cases were excluded. 39 cases were included in the control group. **Conclusion:** Babies born to mothers on Methadone protocol have statistically significantly higher average of platelet count ( $p=0.001$ , CI=95%) and lower average of HB, and WBC compared to the control group ( $p<$ , CI=95%).

Abbreviations: FBC: Full Blood Count, HVS: High Vaginal Swab, GBS: Group B Streptococcus, CRP: C Reactive Protein, Hb: Haemoglobin, WBC: White Blood Cell Count, Plt: Platelet Count, T-STAT: Student's T test, CI: Confidence Interval, IL6: Interleukin 6

## INTRODUCTION

Thrombocytosis and increased circulating platelet aggregates may be factors in the pathogenesis of the focal infarcts, and subarachnoid and germinal plate haemorrhages, described at autopsy in infants of polydrug users' mothers [1].

## MATERIALS AND METHODS

The objective of this study is to identify the relationship between the maternal use of methadone and early neonatal thrombocytosis during first week of life in full term babies.

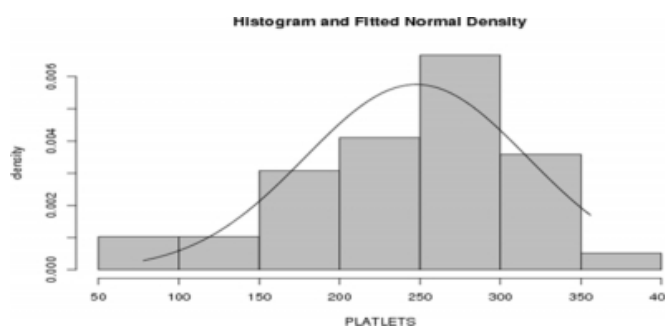
We designed a retrospective cohort study of full term babies whose mothers were on the methadone programme and were not known to abuse other recreational drugs in pregnancy. All babies in our study were born at Princess Royal Maternity Hospital in Glasgow between 01/2006-01/2007 inclusive. FBC for both the study and the control groups were performed for different indications during the first week of life (jaundice, jitteriness, maternal prolonged rupture of membranes, maternal positive HVS for GBS, or maternal pyrexia). Only babies who were full term at delivery, with normal CRP ( $<6$  mg/l), and negative blood culture (no bacterial growth) were included in the study.

## RESULTS

181 babies were born to methadone users. 62 babies fulfilled the criteria of the study. 119 cases were excluded (18 babies were premature, 57 were born to mothers using other drugs with the methadone, and 44 babies did not have any blood test during their hospitalisation). 39 cases, with the same study group criteria, were included in the control group.

### Figure 2

Graph 2: Distribution of platelet count in the control group



**Figure 3**

Table 1: T Test to compare between the means of platelet counts of the study and control groups : twotailed distribution P= 0.001, Significant deference in means

Population Mean Test - Ungrouped Data	
Statistic	Value
Plt mean in control group	247.74358974359
Plt mean in study group	317.4032258
T-STAT	3.35905
p-value	0.001352

**Figure 4**

Table 2: T Test to compare between the means of HB of the study and control groups. two-tailed distribution

Population Mean Test - Ungrouped Data	
Statistic	Value
Hb mean in control group	19.4
Hb mean in study group	18.2
T-STAT	2.33
p-value	0.022

**Figure 5**

Table 3: T Test to compare between the means of HB of the study and control groups. two-tailed Distribution.

Population Mean Test - Ungrouped Data	
Statistic	Value
WBC mean in control group	17
WBC mean in study group	13.9
T-STAT	3.13
p-value	0.0023

{image:5}

## CONCLUSION

There is significant difference in means. Babies to mothers on Methadone protocol have higher average of platelet counts comparing to control group(  $p=0.001$ ,  $CI=95\%$ ). On

the contrary, the mean of HB, and WBC in the control group is significantly higher( $p=0.02$ ,  $p=0.002$  respectively,  $CI=95\%$ )

## DISCUSSION

Thrombocytosis has been reported to occur in the offspring of female mice receiving methadone, whereas it has not been documented in adult mice or adult humans following the withdrawal of methadone [2] .

In the neonatal period, essential thrombocytosis is extremely rare [3], and most high platelet counts in childhood are the result of secondary thrombocytosis [4,5]. Maternal drug abuse has been reported to be one cause of secondary thrombocytosis in infants [6]. However the impact and the management of the neonatal thrombocytosis are not very well studied yet.

There are speculations that the high incidence of Sudden Infant Death Syndrome (SIDS) in this group of patients could be explained by thromboembolic complications in some of the cases [7].

Garcia-Algar et al suggested monitoring of the platelets count till the 2nd week of life [8]. On the other hand, Severe thrombocytosis over  $800 \times 10^9/l$  was reported to be treated with dipyridamole (2 mg/kg/day) which was started on day 15 for prevention of thrombotic complications [3] .

We think that the mechanism of secondary thrombocytosis in newborns differs from that of childhood thrombocytosis, In secondary thrombocytosis of various causes, serum IL6 and C reactive protein concentrations are often significantly increased [9-12]. Serum erythropoietin concentration, which is usually high in iron deficiency anaemia, may contribute to thrombocytosis during human recombinant erythropoietin treatment for anaemia of prematurity [11].

A report of increased thrombopoietin concentrations preceding thrombocytosis in an inflammatory disorder, Kawasaki disease, suggests the possibility of increased thrombopoietin concentrations during the prenatal/perinatal period [11]. The IL6 was depressed and the Thrombopoietin was normal in a case report of neonatal thrombocytosis resulting from the maternal use of non-narcotic antischizophrenic drugs [6]. However, these were measured in the second week of life, not during the early days. The same case showed normal myeloid and erythroid precursors with an increased number of megakaryocytes in bone marrow aspirate [6]. Hanssler L et al did a retrospective

study where they analysed clinical findings and hematological data of 16 neonates born from mothers using methadone and other drugs during pregnancy [7]. all infants showed thrombocytosis after the first week of life comparing to a control group of 18 babies [7]. However, our study shows that this phenomenon takes place in earlier stage, which suggest that antenatal factors may stimulate the megakaryocytes. The relationship between WCC, HB and maternal use of Methadone is not well studied in literature. However, we think that the stimulation of the megakaryocytes could be the reason for the significant difference in WCC and HB between our two groups.

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